Associated factors with Hepatitis B virus infection after 39 years of Expanded Program on Immunization in Central region, Vietnam

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Associated factors with Hepatitis B virus infection after 39 years of Expanded Program on Immunization in Central region, Vietnam

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A Master's Thesis

Submitted to the Department of Global Health Security, Division of Global Health Security Detection Program and the Graduate School Public Health of Yonsei University in partial fulfillment of the requirements for the degree of Master of Public Health

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December 2020

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DECLARATION

I, **Vo Thi Linh Dan,** do hereby declare that the thesis entitled **" Associated factors with Hepatitis B virus infection after 39 years of Expanded Program on Immunization in Central Region, Vietnam"** is the result of my work except as cited in the references. The thesis has not been accepted for any degree and is not concurrently submitted in the candidature of any other degree.

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Vo Thi Linh Dan

South of Korea, December 10th, 2020.

FOREWORDS

First and foremost, I want to thank my advisor - Heejin Kimm. It has been an honor to be her Master's student. I appreciate all her contributions of time, ideas to make my Master's experience productive and stimulating.

For this thesis, I would like to thank my reading committee members: Sunjoo Kang, Euisook Kim for their time, interest, and helpful comments.

Regarding Pasteur Nha Trang Institute, I thank Director Do Thai Hung, who created all favorable conditions for me on doing the thesis. Other past and present members of Infectious Disease Department, that I have had the pleasure to work with.

I would like to acknowledge honorary members from National Center of Global Health and Medicine, Dr. Kenichi Komada and Dr. Hachiya Masahiko approved me to use a part of data, spent their time, and gave me good advice for my thesis.

I am especially grateful for KOICA program and its staff in Vietnam and Korea, who gave me an opportunity and draw a great path on my science journey ahead.

My time at Yonsei was made enjoyable in large part due to the many friends and groups that became a part of my life. I am grateful for the time spent with my roommate-Hongkham Xayavong and friends, for my backpacking buddies and our memorable trips into the mountains and seas, and many other people and memories. My time at Yonsei was also enriched by the sources of precious knowledge from all of the professor of Graduate School of Public Health, Yonsei University, have contributed immensely to my personal and professional time.

Lastly, I would like to thank my family for all their love and encouragement. For my parents, Vo Van Dinh and Tran Thi Lan Huong, who raised me with sincere love and supported me in all my pursuits, always willing to listen and share all my difficulties. And most of all for my loving, supportive, encouraging, and patient fiance' - Nguyen Que Chau, whose faithful support during the stages of this Master is so appreciated. Thank you.

Vo Thi Linh Dan

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December 2020

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ABBREVIATIONS AND ACRONYMS

AHB	Acute Hepatitis B
HBV	Hepatitis B virus
LMICs	Low and middle- income countries
EPI	Expanded Program on Immunization
GAVI	Global Alliance for Vaccines and Immunizations
STI	Sexually Transmissible Infections
SBA	Skilled Birth Attendance
IDR	Institutional delivery rates
HepB-BD	Hepatitis B birth dose
HBsAg	Hepatitis B surface antigen.
WHO	World Health Organization
CHB	Chronic Hepatitis B

ABSTRACT

Background: Hepatitis B infection has been emerging without warning and quickly spread in our globally connected world, considered a noticeable health issue. Vietnam is contemplated as a highly endemic of chronic hepatitis B, which contributes factor to the most common cause of cancer death. Prevention and control HBV in Vietnam mostly depending on the immunization program and regular HBsAg screening. This study aimed to evaluate the efficiency of Hepatitis B vaccination implementation period of EPI in Vietnam from 1981-2019. **Method**: a cross-sectional study, population-based was performed from 4 provinces in Central Region, Vietnam (Khanh Hoa, Binh Dinh, Quang Ngai, Ninh Thuan). Data was collected from 2075 participants from 1-39 years old in June to July 2019 by statra classification method and random selection. Participants were interviewed about geography demographic, environmental and attitude factors, and testing HBsAg (+) through a quick test, which affected their HBV infection status. **Results:** Our study found out the association between the prevalence of HBsAg(+) with age- groups (<18 years old (OR: 0.228, 95% CI: 0.145-0.359, p<0.001); attendant for delivery, including: medical staff (OR: 0.489, 95% CI: 0.330-0.725, p<0.001); traditional birth attendant (OR: 2.015, 95% CI: 1.321-3.076, p=0.001); family member & relatives (OR: 1.891, 95% CI: 1.087-3.289, p<0.05); reason to choose delivery place : Individual selection (OR: 2.264, 95% CI: 1.045-4.904, p<0.05); family member have Hepatitis B: No (OR: 3.861, 95%CI: 2.079- 7.171, p<0.001;); Unknown(OR: 0.518, 95% CI: 0.30-0.895, p<0.05); vaccination history: Unknown (OR: 4.739, 95% CI: 1.808-12.422, p<0.05) and availability of immunization cards: No (OR: 2.988, 95%CI: 1.300-6.867, p<0.05;).**Conclusion**: Hepatitis B infection was still a significant cause among children younger and adults from 1-39 years old in Vietnam. In the context of low vaccine proportion or uncertain their historical vaccination, and the HBsAg (+) prevalence is mostly in the adults; getting a full schedule of Hepatitis B vaccine and checking the status are very important, in particular, population who have not had a chance to approach vaccination due to their external condition during their childhood and their behavior compared to children. There is a need to consider the community communication to vaccinate frequently in the Expanded Program on Immunization within this dramatic situation.

Keywords: *Hepatitis B, Central RegionVietnam, Expanded Program on Immunization*

CHAPTER 1
INTRODUCTION

Hepatitis B infection has been emerging without warning and quickly spread in our globally connected world, considered a noticeable health issue. There are acute and chronic hepatitis B, modified from a wide range of illnesses from asymptomatic to symptomatic, progressive disease[1]. Worldwide, there was an estimated over two billion people infected with hepatitis B and 360 million chronically infected persons[2, 3]. The burden of chronic HBV stands high disproportion in low- and middle-income countries (LMICs), particularly in Asia and Africa[4]. At the present, there is no specific treatment hepatitis B then all of the expenses from treatment were a dramatically vast health finance problem toward the national economy and patients out of pocket. In China, the huge direct cost spending on HBV- related diseases accounts for 30,72% to 297,85% out of annual family income for acute Hepatitis B and primary liver cancer respectively[5]. It also occurs in developed countries like South Korea, during the 2008-2011 period, the amount of economic cost for hepatitis B rose significantly, from US $501.4 million to US $607.8 million. The roundabout cost approximated around 53.4% out of this total[6]. Besides, the chance to approaching health care system is a considered issue for developing countries, especially in the mountainous and rural areas where residents have a few occasion to enter because of environmental factors.

Hepatitis B can be prevented by vaccination and is therefore incorporated in routine vaccination or mass vaccination programs in many countries. With support from Expanded Program on Immunization (EPI), established by the World Health Organization (WHO) in 1974 to support countries uptake of vaccines against Hepatitis B has been increased.

Many studies have found the relevance between HBV and age. The young have a higher prevalence of illness than adults, to be specific the percentage of those infected perinatally, in early childhood, and after age five years are 90%, 30%, 60% respectively[3]. According to Susan Goldstein's study in infants with administration of birth dose is a

material effect on the proportion of HBV related death prevented [7]. Moreover, routine hepatitis B vaccination of infants plays a key role in the process of reducing the morbidity at the young age without birth dose, which would prevent up to 75% of death globally. With 100% complete vaccine series coverage and 100% of infants receiving a birth dose of vaccine, it would be theoretically possible to prevent 95% of all HBV- related deaths[7].

Vietnam is contemplated as a highly endemic of chronic hepatitis B, which contributes factor to the most common cause of cancer death. There was an estimation in chronic infection prevalence of HBV among adults from 8-20% [8-11]. It also referred to this figure of infant, children (4-5 years), adolescents (14-15 years), and adults (25-39 years) were 12%, 18%, 29% and 19%, respectively in a survey of two districts in Thanh Hoa Province in1998 [12].

Prevention and control HBV in Vietnam mostly depending on the immunization program and regular HBsAg screening. At the moment, this duty is being in charge and funding by government and international organizations. Hepatitis B disease will put a load of burden on community health in Vietnam in upcoming if appropriate intervention is not used promptly and properly. Establishment of a national strategy for HBV prevention and control is crucial to develop and implement effective interventions[13]. Despite the effectiveness of HBV vaccine introduced around 3 decades ago, Vietnam is classified as a high burden country regarding HBV which is one of the most popular and dangerous etiology of liver disease.

The number of provinces implementing hepatitis B vaccination has increased over the years from 29 provinces in 1998 to 42 provinces in 2000. Since 2003, with the support of the GAVI organization, the Hepatitis B vaccine has been deployed to children under 1 year old in routine vaccination with 100% of districts nationwide covered. From 2006 up to now, the rate of vaccination for hepatitis B with 3 doses in children under 1 year old has always reached over 90%, except in 2007, which was low due to lack of vaccines.[14] In 2010, the EPI program carried out a survey on "Evaluation of the efficacy

of Hepatitis B vaccination in the 2000-2008 period", thereby determining the prevalence of HBsAg infection in Vietnamese children. The survey was conducted in 51 provinces / cities with over 7,000 children born between 2000 and 2008. The results showed that having HBV vaccination significantly reduced the proportion of children with HBsAg ($p < 0.05$) compared to the group of children not receiving the injection. Besides, the vaccination with the basic dose (3 doses) significantly reduced the rate of children carrying HBsAg ($p < 0.05$) compared with the group of children who had not received enough shots (1 or 2 shots). In particular, the survey results show a marked decrease in the prevalence of HBV virus among groups of children born in the period 2000-2008. The group of 5-year-olds at the time of the survey (born 2006) had a hepatitis B virus infection rate of 1.89%, achieving the WHO target of reducing the rate of hepatitis B virus infection among 5-year-old children. to below 2% in 2012 and work to reduce this rate to below 1% in the future.[14]

A significant achievement was established in Expanded Program on Immunization (EPI) in Vietnam, while the country experienced repeated disease outbreaks. Nguyen Van TT's study showed the prevalence of current HBV infection - HBsAg(+) has found extent from 10% to 20% in the general population and 20% to 40% among injecting drug users and HIV positive patients[13]. The prevalence of chronic HBV infection is 8–20% and 31–54% among the general and the urban high-risk populations, respectively [15]. Various projects and modeling studies predict around 8 million chronic HBV cases and approximately 58,600 HBV related liver carcinoma in Vietnam by 2025. It is also estimated the HBV-related death will be 40,000/year by 2025 [10, 16, 17].

Since the country introduced hepatitis B vaccination, modification of HBsAg prevalence has not been investigated by a population-based survey previously. Therefore, we investigated the influence of the expanded immunization program through this topic: "**Associated factors with Hepatitis B virus infection after 39 years of Expanded Program on Immunization in Central Region, Vietnam."** in 2 age group under 18 years old and over 18 years old with hypothesis: "< 18 years old groups's HBsAg (+) was lower

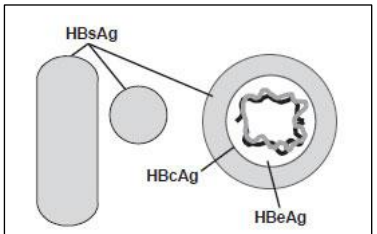
than those of ≥18 years old age group thanks to EPI “, due to the high probability of transmission from mother to children in their age of reproduction. Moreover, we also want to compare the efficiency of Hepatitis B vaccination to community after the melioration of EPI (1998-2000). The evaluation of HBsAg positive prevalence in children and adults among the representative population in four provinces (Khanh Hoa, Ninh Thuan, Binh Dinh, and Quang Ngai) in Central Region, Vietnam which may contribute to understanding disease epidemiology, valuable information to assess the effectiveness of preceding vaccination, formulating future immunization policy and use it for preventive measures in the future as well as finding the relation among prevalence of Hepatitis B immunization and other factors.

CHAPTER 2
LITERATURE REVIEW

2.1. HEPATITIS B VIRUS OVERVIEW

2.1.1. Hepatitis B Virus Concept

There are five categories hepatitis (A, B, C, D,E) in which hepatitis B- formerly called serum hepatitis, is one of the most hazardous infectious diseases out of these. HBV is a small, double-shelled virus, belongs to the family of Hepadnaviridae and has been recognized as separate entities since the early 1940s and can be diagnosed with specific serologic tests. It may take place with AHB infection (coinfection) or HBV carrier (superinfection)[18]. According to Lok et al in Chronic Hepatitis B (2001), the HBV genome is frame as a relaxed circular, partially double-stranded DNA of approximately 3,200 base pairs. The open reading frames encoding the envelope (pre-S/S), core pre-core/core), polymerase, and X proteins are partially overlapped [19, 20] in which the large (L), middle (M), and small (S) surface glycoproteins are encoded by pre- S/S open reading frame.



(Source: Center for Diseases Control and Prevention)

Figure 1. Hepatitis B Virus

2.1.2. Hepatitis B Classification

2.1.2.1. Acute hepatitis B

AHB happens when a person is first infected with hepatitis B. Adults often experience clinical signs and symptoms more than infants or children where the prevalence of developing symptoms in infants, children from 1 to 5 years old and older children and adults are less than 5%, 5-15%, 33-50% respectively [21]. Especially, adults usually have an asymptomatic acute course, though this figure was just approximately 50% out of AHB patients. Most cases in healthy people who was infected, do not express any symptoms and exclude virus following natural recovery and active adaptive immunity of body. HBsAg and the production of anti-HBs will eliminate completely in several months later and create

immunity to future infection. In the contrast, if infected body can not get rid of the virus after six months turn out it will progress to CHB. There is only 1-2% caused of fulminant hepatitis with a numerous of injured liver cells and get change of fatal. It estimated around 200-300 Americans death caused by fulminant disease each year (case-fatality rate 63% to 93%)[18, 22].

It is undifferentiated clinical course among types of acute viral hepatitis, including AHB. The incubation period ranges from 45 to 160 days (average, 120 days). Before the onset of jaundice 1 to 2 days, several initial nonspecific symptoms like malaise, anorexia, nausea, vomiting, right upper quadrant abdominal pain, fever, headache, myalgia, skin rashes, arthralgia and arthritis, and dark urine appear. It is called preicteric, or prodromal phase, which takes place around 3 to 10 days. Jaundice, light or gray stools, hepatic tenderness and hepatomegaly (splenomegaly is less common) represent for icteric phase, which is variable but usually lasts from l to 3 weeks. Malaise and fatigue may maintain during convalescence for weeks or months, while other symptoms disappear. Blood testing identifies clearly AHB infection through the positivity of HBsAg, anti-HBc, IgM anti- HBc and negativity of anti- HBs [18].

2.1.2.2. Chronic hepatitis B

Chronic hepatitis B is chronic inflammatory disease of the liver caused by persistent infection with the existence of HBV for more than six months (after their first blood test result). It is considered as a high risk cause of liver diseases. HBeAg-positive and HBeAg-negative are classified into two subgroups of chronic hepatitis B [18].

CHB patients may not recognize their disease due to frequently asymptomatic status, which enhances the high risk of infecting others and has been referred to as carriers. The proportion of chronic HBV- related diseases such as chronic hepatitis, cirrhosis, liver failure, and hepatocellular carcinoma is prevalent, in which 25% of deaths prematurely from cirrhosis or liver cancer. There is 25% of carriers acquire chronic active hepatitis, result in cirrhosis. Comparing to CHB infected persons, noncarriers experienced the low risk of hepatocellular carcinoma, at 12 to 300 times [18].

2.1.3. Transmission of Hepatitis B

2.1.3.1. Reservoir

Human is known for the only host for HBV, although other primates have been infected in laboratory conditions. Until now, there is no evidence about the existence of HBV in animals, insect hosts, or vectors [18].

2.1.3.2. Transmission

The proportion and patterns of transmission are different from parts of the world. The high prevalence chronic HBV infection which accounted for greater than 8% HBsAg positive in general population is 45%, while this figure for moderate prevalence areas (2% to 7% of the population is HBsAg positive) and a low prevalence (less than 2% of the population is HBsAg positive) are 43%, 12% respectively.

The way of HBV's transmission through perinatal, percutaneous, sexual exposure and close contact between persons by open cuts and sores with HBsAg positive body fluids from persons who have HBV infection (acute and chronic), especially among children in hyperendemic areas [18, 23-26].

It is also classified into horizontal transmission and vertical transmission. Among individuals have high-risk sexual behavior such as unprotected anal and vaginal sex or persons who use contaminated injecting devices together experience the enhanced risk of HBV infection are called horizontal transmission. HBV infection is coinfected with hepatitis C (mostly through using injectable drugs) and hepatitis D (required the presence of HBV), at 10-15%, 5% respectively [27]. Vertical transmission occurs from mother to child (perinatal transmission) at birth or infancy period, which is very efficient. The prevalence of infants may acquired HBV infection from their mother who is positive for both HBsAg and HBeAg reaches 70-90% if they do not have postexposure prophylaxis. If the mother is positive only for HBsAg, the risk of perinatal transmission is about 10%. However, 90% of infant HBV infections will progress to chronic infection[18].

The level of HBV density is different, the highest concentration are in blood and serous fluids, while in other fluids like saliva, tears, urine, and semen are lower titers [28]. There is no clear proof for HBV transmission from person to person via tears, sweat, urine, stool, or droplet nuclei.

HBV can survive outside the body for prolonged periods. The transmissible capacity of HBV remains at least 7 days on environmental surfaces through open cut or sore, even without the visible blood [29, 30]. Injection-drug use plays an important mode of transmission, without overt needle puncture, break in the skin like fresh cutaneous scratches, abrasions, burns, or other lesions, may also be a convenient entry.

Nosocomial exposures like transfusion of blood or blood products or hemodialysis, use of meters and lancets for glucose monitoring, insulin pens, and needle-stick or other "sharps" injuries sustained by hospital personnel have all resulted in HBV transmission.

Few cases in which transmission from HBsAg-positive health care personnel to patients has been documented, particularly since implementation of standard universal infection control precautions [31]. In many countries, the proportion of HVB transmission among patients in dialysis centers is high due to failure to adhere to recommended infection control practices against transmission of HBV and other blood-borne pathogens in these settings. IG, heat-treated plasma protein fraction and albumin are viewed as protected. Before, outbreak have been followed to tattoo parlors, acupuncturists, and barbers.

2.1.4. Laboratory feature and Diagnostic criteria

Diagnosis is cooperation among clinical, laboratory, and epidemiologic discoveries. Not only clinical symptoms can represent for HBV infection but also definitive diagnosis relies upon the results of serologic testing. There is a modification of presence of the serologic maker between acute and chronic HBV infection. HBsAg can be found in blood and body fluids for 1–2 months before and after the onset of symptom. HBsAg is the most usually utilized test for diagnosing acute HBV or detecting carriers within 1 or 2 weeks in early-stage or 11 to 12 weeks later after exposure to HBV when

sensitive assays are used. Whether acute or chronic HBV infection, there always has the appearance of HBsAg. Similarly to HBsAg, the presence of anti- HBc (core antibody) in all of HBV infection, appears shortly after HBsAg in AHB but it is not a serologic marker for acute infection. Anti-HBc reminds of an infected HBV indeterminate time in the past. There is no appearance of anti- HBc in person who receives HBV from hepatitis B vaccine.

Figure 2. Interpretation of Hepatitis B Serologic Tests [18]

Test	Result	Interpretation	(*)Postvaccination testing, when it is recommended, should be performed 1-2 months following dose #3. (a) 1. Maybe recovering from acute HBV infection. 2. Maybe distantly immune and test is not sensitive enough to detect a very low level of anti-HBs in serum. 3. Maybe susceptible with a false positive anti-HBc. 4. Maybe chronically infected and have an undetectable level of HBsAg present in the serum.
HBsAg Anti-HBc Anti-HBs	Negative Negative Negative	Susceptible	
HBsAg Anti-HBc Anti-HBs	Negative Negative Positive with ≥10mIU/mL*	Immune due to vaccination	
HBsAg Anti-HBc Anti-HBs	Negative Positive Positive	Immune due to natural infection	
HBsAg Anti-HBc IgM Anti-HBc Anti-HBs	Positive Positive Positive Negative	Acutely infected	
HBsAg Anti-HBc IgM Anti-HBc Anti-HBs	Positive Positive Negative Negative	Chronically infected	
HBsAg Anti-HBc Anti-HBs	Negative Positive Negative	Four interpretations possible[a]	

2.1.5. Treatment and Prevention - Role of vaccination

2.1.5.1. Treatment

Although there are plenty of efficient medicine can control and even stop the development of HBV from further damaging a liver, treatment is supportive. There is no specific treatment for AHB [32].

Interferon alpha (IFNa, or PEG-IFNa) and nucleoside or nucleotide analogs (lamivudine, adefovir, entecavir telbivudine, and tenofovir) are considered as two major groups of antiviral treatment, have been licensed for the treatment of chronic HBV infection in many countries. Depending on the physical conditions of CHB patients, all of decision to treat or choosing the appropriate therapy has made. The progress of considering, choosing the appropriate of therapy or treatment depends on individual status of chronic HBV infection. Patients with HBV DNA levels above 2000 IU/ml, serum alanine aminotransferase levels above the upper limit of normal, and severity of liver disease assessed by liver biopsy (or non-invasive markers once validated in HBV-infected patients) generally are considered for treatment showing moderate to severe active necroinflammation and/or at least moderate fibrosis using a standardized scoring system[18].

It is a costly payment for prolonged treatment to maintain suppression of viral replication in both developing and developed countries. However, medications have significant side effects that require careful monitoring. Combination of therapy are been considering in study, but it is likely to reduce the appearance of virus mutants resistant to treatment. Overall, there are promising new drugs in the future which can control and even cease the hepatitis B infection as well as further damage and complications.

2.1.5.2. Prevention- Role of vaccine

2.1.5.2.1. Vaccine

Apart from another preventive methods such as reducing the horizontal transmission from person to person through blood and other potentially infective body fluids, which is highly recommended to avoid blood donation and sharing personal hygiene

tools (toothbrushes, razors,..) with household members in AHB or CHB infection or in the hospital setting, patients with HBV infection should be managed with standard precautions. Hepatitis B vaccine plays an important role in the worldwide prevention strategy.

Hepatitis B vaccine was launched in United State since 1981 which have had a large effectiveness on AHB disease although it is less optimal on CHB disease. However, there are so many impact on dramatic reducing complications such as HCC in Alaska Natives [18] and the successful influence of immune program on infants, children and adolescents about the prevalence of AHB and then CHB [33]. There are multiple formulations (Recombivax HB and Comvax, Merck; Engerix-B, Pdiatrix, and Twinrix, GlaxoSmithKline) are now licensed in the United States, which products from yeast (*Saccharomyces cerevisiae*) and recombinant techniques to generate the hepatitis B surface antigen (HBsAg) protein [34].

A variety of strategies to reduce the prevalence of HBV universal, especially concentrate on the target population in 2011[18] such as prenatal testing of pregnant women for HBsAg to indicate a proper immunoprophylaxis for prevention of perinatal infection in infant and contacts, a routine vaccine for infants, adolescents, adults at high risk for infection. However, it still remains three major risk groups (heterosexuals with multiple partners or contact with infected persons, injection-drug users, and men who have sex with men) can not reach the impact of immunization program. The most implicit reasons of these groups are lack of awareness about risk of HBV infection and its complications and consequence, lack of effective public or private sector programs, and vaccine cost. Accessing to these population is considered a problem [18].

HepB-BD considers as an important key factor in reducing the prevalence of HBV infection and the proportion of HCC. The first plasma-derived hepatitis B immunization was licensed in USA in 1981 which was replaces in 1986 and by recombinant HBV vaccine in 1989[35]. The amount of antiHBs antibodied in greater than 95% in infants who vaccinated completely hepatitis B vaccine series including birth dose plus two additional

booster doses[36]. According to WHO's recommendation that HepB-BD should vaccinated as soon as possible after birth, better within 24 hours, to prevent perinatal HBV transmission. The birth dose still remains its effectiveness if given after 24 hours, although comparing to this monovalent HBV within this time, it has less significant impact[37]. Two subsequent booster doses such as monovalent hepatitis B vaccines or HBV containing combination childhood vaccines should followed the HepB-BD. Mainly, birth dose for infants as well as Hepatitis B immunization for children are currently recommended in many countries. However, 186 countries did not conduct the HepB-BD within 24 hours of birth although universal vaccination has been introduced nationwide since 2017[38] .There was 79% of the 192 WHO member states adopted policies of universal childhood immunization against HBV in 2003[39, 40]. A significant achievement of the associated benefit was the decline in the prevalence of neonatal HBV infection and subsequent sequelae in Taiwan after the introduction and widespread use of HBV vaccine[41-43].

According to CDC, the recommended dose for infants and children younger than 11 years old are 0.5 mL (5 mcg) of pediatric or adult formulation Recombivax HB (Merck) or 0.5 mL (10 mcg) of pediatric Engerix-B (GlaxoSmithKline). The usual schedule is 0, 1 to 2, and 6 to 18 months with three intramuscular doses of vaccine, but depending on individual country and infectious disease prevalence, they will give another suitable immunization schedule. Toward mothers have HBsAg positive or unknown HBsAg status, their infant will receive the last dose by 6 months of age (12 to 15 months if Comvax is used).

Hepatitis B vaccine and hepatitis B immune globulin (HBIG) within 12 hours of birth are suggested for preterm infants whose mother have HBsAg-positive or unknown HBsAg status. Although preterm infants whose weight less than 2000 grams have a lower response to hepatitis B vaccine administered before 1 month of age, they are likely to reach an adequate response as full-term infants by chronologic age 1 month, regardless of initial birth weight or gestational age. Besides, those infants who have mothers are HBsAg negative, can receive the first dose of the hepatitis B vaccine series at chronologic age 1

month. If preterm infants are guaranteed about their stable medical status and gaining weight consistently before chronologic age 1 month, they also can receive hepatitis B vaccine. The full doses are recommended without divided or reduced doses.

Vaccination program influenced to the population has been shown in in the WHO Western Pacific region, where followed the timebound target with the first deployed HBV vaccination programs in the 1980s and 1990s in several countries [44] .All of countries and areas of the Western Pacific region had started vaccinating infants by 2005, which estimated the number of CHB infection among children born between 1990 and 2014 in this region [45] prevented by Hepatitis B vaccine was more than 37 million cases, in result averting more than 7 million deaths related to HBV. The percentage of HBV threedose vaccination coverage and HBV birthdose coverage were 92.2% and 81.5% respectively in 2014 [45]. As of 2015, the prevalence of HBsAg primarily decreased from 4.7 % to 1.3% in children under 5 years old as an accomplishment of worldwide vaccination programs whereas there was no change in this prevalence in nonvaccinated people [46]. Hepatitis B vaccine for infants has been used in 186 countries and three doses of HBV vaccine coverage was estimated to be 84% by the end of 2016 [27].

The vaccination program, which should be flexible and should take into account the feasibility of delivering three doses of vaccine to adolescents and adults, has not been existing in routinely schedule for this age group. However, unvaccinated adults and adolescents should be immunized whenever possible. High-risk groups are recommended for identifying and receiving hepatitis B vaccine including drug users and persons with multiple sex partners, hemodialysis patients,hemophiliacs, household and sexual contacts of persons infected with HBetcct,…. [18, 47]. There was universal screening for pregnant women in 1988 after the defeat in recognizing hepatitis B infected in high risk women [26] , though it did not shown the breakthrough impact on reducing HBV infection rate [48].

2.1.5.2.2. Immunogenicity and Vaccine Efficacy

It estimated a greater number of 90% of healthy adults and more than 95% infants, children, and adolescents (from birth to 19 years of age) will get fulfillment of antibody

responses. Immunogenicity reduces at an age-specific, to be clarified recipients respond to a three-dose series around 90%(after 40 years old) and 75% (by 60 years old) respectively.

For who receives the adequate vaccine series, the range of preventing infection or clinical hepatitis is from 80-100%.

Toward most hemodialysis patients and immunocompromised persons, larger vaccine doses (2 to 4 times the normal adult dose), or an increased number of doses, are required to induce protective antibody.

Injection site is also a crucial part in enhancing the vaccine efficacy. The highly recommended muscle for hepatitis vaccination in adults and children is deltoid muscle, while this site for for infants and neonates is the anterolateral thigh. It indicates the lower immunogenicity of vaccine in adults when injections are given in the gluteus. Apart from these site, Hepatitis B vaccine should not be counted as valid and should be repeated unless serologic testing indicates that an adequate response has been achieved.

2.2. EPIDEMIOLOGY OF HEPATITIS B IN WORLDWIDE AND VIETNAM

2.2.1. Epidemiology of hepatitis B in worldwide

Hepatitis B is considered as an important issue for many countries worldwide in the light of its consequence to human's health and significant effects to social economy with high treatment cost. HBV- related deaths was booming from 0,89 to 1,45 million just in two decades starting from 1990[49]. The number of deaths from viral hepatitis was 1,32 million(2015) due to its complications accounted for 96%, quite equal to this figure in tuberculosis(1,37 million) and higher than HIV infection (1,06 million) and malaria (0,55 million). HBV is responsible for the majority problem 1,34 millions viral hepatitis deaths, at 66%[46]. According to WHO, 887.000 deaths (2015) from HBV mainly caused by complications as cirrhosis and hepatocellular carcinoma [50].

Globally, HBV concentrated in Africa and Asia -Pacific regions, parts of the Middle East and the Amazon Basin, 8-15% of the population carry HBV with over 60% lifetime risk of HBV infection. The most prevalent transmission in those areas are acquired

at birth or during early childhood. The rate of chronic liver diseases among adults are very high but the acute HBV – related disease is rarely because of asymptomatic of infection [18, 32]. In Asia, the prevalence of HBsAg were high or high intermediate in general population in Vietnam, Mongolia, Laos, China, the Philippines, South Korea, Singapore and Cambodia[2]. China's report following a national serological survey in 1992 indicated the prevalence of HBsAg in total residences was 9,75%[51], which the majority transmission were mother to child and other non-parental exposure during early childhood [52]. 181.826 prenatal infections was estimated in this region in 2014, in which 90% out of this figure was diagnosed chronic, in particularly 35% (63,709 cases) occurred in China, 33% (60,753 cases) occurred in the Philippines, 23% (42,363 cases) occurred in Viet Nam, and 4% (6804 cases) occurred in Papua New Guinea [45]. It was also estimated more than 300 thousand deaths per year in the Western Pacific Region in 2017 [53] and stood in the highest position in the prevalence of HBsAg (6,2%) comparing to others continents, which included nearly 50% people with chronic hepatitis B infection globally [46, 54].

Whereas, this figure in Europe and the Americas experienced a lower chronic HBV carrier prevalence from 0.1-0.5% in general population, with lifetime risk of HBV infection less than 20%, basically concentrate on adulthood [18, 32]. Annually in America, the number of patients' deaths in light of hepatitis B-related cirrhosis and hepatitis B-related liver cancer are 3,000 to 4,000 and 1,000 to 1,500 respectively [18]. Although, Europe and the Americas experience the lower prevalence of HBsAg, this figure does not describe exactly contribution equally among areas and ethnic groups, mostly prevalent in the African and Asian immigrants, or their regular residence. Moreover, those certain groups may transmit to other indigenous population groups through sexual contacts such as men who have sex with men, persons with multiple sex partners and injecting drug users. Thus, making quality and accurate assessment of the national prevalence is much more challenging [49].

Until now, there is no specific treatment for hepatitis B and the number of people who can approach the existing treatment is quite rare. The main remedy to eliminate the

proportion of HBV- related morbidity and mortality, its consequence as well as block the dramatic spreading out of HBV infection worldwide is prevention. Hepatitis B immunization has deployed popularly in every regions to fulfill this intervention mission. Borne-blood transmission can be reduced completely by the birth dose vaccination, intravenous hepatitis B immunoglobulin, and peripartum antiviral therapy for mothers with high viral load [55, 56]. Besides, potentially effect of hepB-BD also helps newborns out of the HBV infections [57].

There were many remarkable achievements in hepatitis B immunization program. According to Weisen et al's study, before hepatitis B immunization program, chronic HBV infections accounted for greater than 8% in most of countries and plummeted to less than 1% in most countries in Western Pacific Region by 2014. In the period of 10 years since 2000, the number of the 3rd dose of HBV immunization and HepB-BD went up dramatically and became stable in the past decade. It showed the decrease in the prevalence of chronic HBV infections among babies annually (~37.595.665 cases) between 1990 and 2014 by vaccination program. The statistic reported 92.2% HepB3 coverage and 81.5% HepB-BD coverage on average with 2.999.996 chronic infections and 570.566 deaths would have occurred in their lifetime were averted in 2014. However, a few countries in this region should exert themselves in reducing the prevalence of HBV among children while this figure still stood at over 3%[45]. South Korea experienced the extremely terrible past of HBV- related diseases. The prevalence of HBsAg in young generation was high, at 4-5% in the years of 70s and early 80s [58, 59]. Fortunately, this figure went down significantly when government applied initially vaccination program in Korea by 1985; from 3.2% (1988) to 2.6%(1993) [60], continued to drop to under 1%(1995) [61] and reached at 0.2% (2006)(KCDC, 2009). The prevalence of positive HBsAg results also have experienced a strongly decline in 20 years since 1986 in men and women, (8.3%, 6.9% respectively)(KDCD, 2012)[62]. Sharing the similar great results after implement the mass of HB vaccination in Russia, the number of AHB cases reduced 33 times from 43.8 to 1.3 over 100.000 population between 1999 and 2014 [63].

In general, hepatitis B vaccination plays a core role and priority choice for public health, though HBV infection is still a burden to many countries, especially for endemic areas such as Asia and Africa.

2.2.2. Epidemiology and Immunization program of Hepatitis B in Vietnam

According to *General Statistics Office of Vietnam – 2015,* the average population of Vietnam was approximately 83.83 million and the density was 252 persons /km2 [64], in which around 8.4 million people lived with chronic HBV and 23.300 HBV-related deaths [65]. There was a high chance of positive HBsAg in community, from 15-20% in a large of areas in Vietnam [8, 12, 66-69]. The proportion of Hepatitis B birth dose is only 74% coverage[70]. There is greater than 8% of Vietnamese population has HBV and 90% children are infected from their mother who has positivity of HBV. In average, one in four adults who acquire this disease as children die of health problems such as cancer liver[71].

The study conducted by Van Nguyen et al. in 2010 reported the highest prevalence experienced in age group of 30 to 39 years in both genders (19.3% for male and 14.0% for female) followed by age group of 40-49 years old (18.6% and 13.4%, respectively) [13]. The amount of HBV exposure accounted for a half in the teenagers (16–19 years), although increasing with age in Van Thi et al. studying in 837 participants of two rural districts in Thai Binh, 2007 [8].

Although vertical transmission is considered common in high endemic nations like Vietnam, horizontal transmission also plays an important role in spreading HBV, specific from mother to children. The prevalence of HBsAg in children was from 9.3% to 14.1%,suggested that perinatal and early childhood [13]. Every year, an estimated 54,600 children have chronic hepatitis B if they do not vaccinate in 24 hours after delivery, who become the important source of infection in community. Around 20-30% children of this figure (~11.000-16.000 children) would evolve in liver cancer and cirrhosis [66]. Furthermore, Vietnam also experiences difficulty from reality conditions like hard approaching areas (mountain, island,etc…), lack of finance for health care, behavior and education level, ethnicity, etc…Nguyen.T. Hien et al estimated the prevalence among

children in Vietnam through his study in 6949 children, which reported overall HBsAg prevalence in target participants was 2,7% (95% CI= 2,20-3,30). This figure was higher in children born at home (5,47%)compared to those born in facilities (2,25%)(PR= 2,43 95% CI=1,68-3,51). Children of other ethnicity had higher HBsAg prevalence than Kinh ethnicity (5,36%, 2,16% respectively) (PR: 2.48, CI: 1.71–3.58) [72].

Hepatitis B virus vaccine is highly priority option for preventing both perinatally and horizontally acquired chronic HBV infection [73-75]. Since 1997, hepatitis B vaccine has been started to utilize in selected areas, then infant hepatitis B vaccine was expanded nationwide in Expanded Program on Immunization in 2002 with an average of 4,5 million doses annually. With the financial support from GAVI Alliance, a monovalent hepatitis B vaccine birth dose was introduced in 2003. Initially, hepatitis B vaccine was recommended to be given within 7 days after birth and changed into 3 days after birth, 24 hours after birth in 2002 and 2006 respectively. The birth dose was given at health facilities only. In June of 2010, subsequent hepatitis B doses are given as part of a pentavalent DPT-Hib-Hepatitis B vaccine was deployed in children under one year old, which made the number of hepatitis B doses reduced to 1,5 million and just only used for neonatal period since 2010. Caregivers were requested to bring their child to commune health center and outreach points (for hard to reach areas only) for vaccination[66, 72].

Vietnam shares the similar fundamental routes of HBV transmission toward other countries in South East and Eastern Asia, are from mother-to-child or from close contacts during early childhood[76]. In collaboration with Ministry of Health, Provincial Department of Health and WHO, Expanded Program implemented with potential effort and determination in order to reduce the mortality of transmission from mother to children in maternal period, enhance the percentage of hepatitis immunization is B vaccine for infant in 24 hours after delivery. There was a significant climb in three-dose hepatitis B vaccine coverage from 24% in 2000 to >90% yearly starting 2004. However, this figure experienced a fall dramatically to 29% in 2007 and 26% in 2008 due to media reports of alleged adverse events following hepatitis B birth-dose administration [77, 78]. In World

Health Organization's Western Pacific Regional meeting in 2012, Vietnam achieved the goal of declining percentage of chronic HBV under 2% in children of 5 years old [66].

Overall, the enlarge of hepatitis B vaccine and accomplishment that EPI had got before, though hepatitis B in Vietnam still remained a serious problem in community health and could be a burden in the future. Vietnam is conquering to decline the prevalence of HBV infection with well policy and effort in immunization program.

2.3. CHARACTERISTICS ABOUT STUDY PARTICIPANTS

Quang Ngai, Binh Dinh, Khanh Hoa and Ninh Thuan are all located in central region of Vietnam, which is a component of three main regions in Viet Nam. It has 15 coastal provinces and 5 mountainous provinces, connected the southern and northern of nation. For many decades, those provinces have suffered from natural disasters, obstacles and difficult of access geography, lack of propitious conditions,etc… for developing themselves. However, with a new policy from government through "Doi moi" period as well as strong self-reliant and taking advantage of province's human and natural resources, those provinces have recent got a very fast, stable, and equitable economic growth to date. They concentrate on exploiting tourism along the coast, seaports, industrial zones, export processing zones and transportation. The traditional of agriculture, fishery, handicrafts have interlocking and supporting activities. As the front of the Mekong sub-region, from here it is possible to trade with countries such as Laos, Cambodia, Thailand, Myanmar and further to South Asian countries and southwestern China through the axis of the East-West corridor, Highway 9, Road 14, Road 24, Road 19. These economic areas not only play a role in driving the socio-economic development of the region but also in the socio-economic development strategy, country geography, economy, politics, culture and national security[79].

Despite the fact that the recent economic growth is potential, central region faces the challenge of further problems, especially health issues are always considered. Comparing to two other regions, central region is considered as a complicated region in health management and EPI with the geographic diversity, demography and sharing border

with other neighbor countries. It still remains the large amount of people living in disadvantage area, especially ethnic minorities who neither have a right health seeking behavior nor chance to approach health system and EPI regularly. Besides, patient's demand for health care service and utilization have changed based on their own income and the dramatic modification in policies in health sector in Vietnam, which may relate to infant vaccination program.

Overall, EPI in general and hepatitis B vaccine in specific is a topic of universal interest, approaching immunization helps governors, community's leader and health manager have a well-round outlook of the current situation aiming to improve not only the health system but also the EPI and enhancing the quality of civil life.

CHAPTER 3
METHOD AND MATERIALS

3.1. STUDY DESIGN

This is a secondary analysis of a population- based, cross-sectional seroprevalence survey, which cooperated between Pasteur Institute Nha Trang and National Center of Global Health and Medicine (NCGM) during June to July in 2019 at the four provinces (Khanh Hoa, Ninh Thuan, Binh Dinh, Quang Ngai) in Vietnam. Data source was received using approval from two aforementioned organizations for conducting.

3.2. METHODOLOGY

3.2.1. Population and Sample size

The residence lived in four provinces (Khanh Hoa, Ninh Thuan, Binh Dinh, Quang Ngai) were chosen randomly and agreed to participate in study. This representative cross-sectional survey sampled population based on a stratified four-stage cluster design. Demographic and vaccination data were collected along with a whole blood specimen that was collected and interpreted in the field with a point-of-care HBsAg test. We estimated the seroprevalence by age group for every 5 years old. The required sample size was calculated by WHO's samples size calculator. (http://www.who.int/chp/steps/resources/sampling/en/)

The sample size of 240 for each age group was calculated based on the expected seroprevalence of 50% (to maximize the size) with a 5% level of significance and a precision of 10.0%. The design effect for cluster sampling was assumed to be 2.0 with a response rate of 80%. The sample size of 1200 households was calculated based on the population pyramid and average number of household members in Vietnam to cover 240 in each group.

- Population in Vietnam (2014): 90,730,000
- Household in Vietnam (2014): 26,700,000
- Average number of household members: 90,730,000 / 26,700,000 = 3.4

- # of households to be visited: 1200
- # of members visited (expectation): 1200 * 3.4 = 4080
- # of members visited by age group

Figure 3. Participants distribution

Age group	Rate(%)	#	Cumulative	Age group	Rate(%)	#	Cumulative
0-4*	8.01	327*	327	40-44	6.57	291	2885
5-9	7.86	321	649	45-49	5.92	268	3153
10-14	7.18	293	942	50-54	5.25	242	3395
15-19	6.80	277	1219	55-59	4.16	214	3609
20-24	7.95	324	1543	60-64	2.66	170	3779
25-29	9.25	377	1920	65-69	1.52	108	3887
30-34	8.67	354	2274	70-74	1.17	62	3949
35-39	7.84	320	2594	>75	2.06	129	4078
				Total	100.00	4078	

* for 1-4 years old, # will be 261 (= 327 * 4/5)

- Expected Total # to be visited (from 1 to 39 y.o.): 2528 (= 2594 – 327 +261)

3.2.2. Sampling method

Collected samples from representative population were aged 1 year old to adults less than 40 years. They were selected by 4 stages probability proportional to size (PPS) sampling. Provinces considered as strata, yielding a total of four strata.

In the first stage of sampling, three districts were selected randomly from each stratum using probability-proportional-to-size (PPS) based on the population data.

In the second stage, two communes were selected randomly from each selected district by PPS, and a total of 24 communes were selected.

In the third stage, two villages were selected randomly from each selected commune by PPS, and a total of 48 villages, as clusters, were selected.

In the fourth stage, 25 households were selected randomly from each selected village, and a total of 1200 households were selected.

All the members from 1 to 39 years old in each selected household were included into the survey. When the number of collected sample in 1 village reach to 54 (= 2594 / 48), the survey team stopped data collection at the village.

Figure 4. Distribution of sample size collecting

Age group	Sample size(n)	Age group	Sample size(n)
1-4	292	20-24	169
5-9	358	25-29	236
10-14	310	30-34	238
15-19	230	35-39	242
Total			**2,075**

(*) Data was collected from 2093 participants, which had:

12 were excluded for analysis (6 are 0, 4 are 40 years old and 2 are of unknown age)

6 were excluded for analysis (no HBsAg testing or unknown results)

3.3. STUDY LOCATIONS AND STUDY PERIOD

3.3.1. Study location

48 villages (24 communes) in four provinces (Khanh Hoa, Ninh Thuan, Binh Dinh, Quang Ngai)

3.3.2. Data collection period: From June to July 2019

3.3.3. Data collection method

3.3.3.1. Data collection equipment

Questionnaire

The structured questionnaires were prepared before the field survey. Toward participants under 18 years old, their parents or caretaker was responsible for complete the questionnaire. Information was collected on the demographic status and immunization history, socioeconomic status of the household as well as the behavior seeking for healthcare service. Questions regarding potential factors for acquiring and treating hepatitis B (e.g., family history, barrier to access the treatment) were added. Questionnaire divided into 3 main components: demographic for every participants; historical vaccination and for ≥ 18 years old participants. The household survey interviewed the respondents to collect information about the socio-demographic characteristics of the households and also detailed information about episodes of illness and the use of healthcare services of each family member recently.

HBV kit test

The blood specimens (approximately 50 mL) was collected by finger prick and was tested in the field using the Alere Determine^{TM} HBsAg point-of-care test strip (reported sensitivity: 95–100%; reported specificity: 96–100%)[80-82]. Eluates were tested for HBsAg using a chemiluminescent microparticle immunoassay (Architect i2000SR; Abbott Diagnostics, IL, USA). The relative light unit (RLU) value of each sample was detected with an automated system. The sample was considered to be positive for HBsAg based on comparisons to the RLU value of a calibration sample.

3.3.3.2. Data collection technique

Step 1: Chose health staff who get familiar with collecting data for scientific study and technicians who were trained blood taking.

Step 2: Surveyors were trained about asking questionnaire, observation in data collection procedure and how to take blood for HBs-Ag testing was conducted in PINT.

Step 3: Trial survey

Chose randomly 10 people from two health care centers and conducted trial survey. After trial survey, evaluated the average of time for interview and finished the questionnaire, changing those of inappropriate questions based on reality residence conditions, capacity of understanding and answering from participants.

Step 4: Collecting data

Surveyors explained the objectives of study and interview participants, followed the questions. Participants had to read sign in consent form. Participants answered questionnaire must be above 18 years old. For who was under 18 years old, their mother, father or guardian helped them answer the questionnaire. After answered questionnaire, participants continued to take blood and receive the result of HBsAg and gifts before leave.

Survey team

Twelve survey teams were formed, and each team was comprised of three members including a health staff from PINT and two surveyors nominated from the district health staff. Each team covered 1 selected district (2 communes, 4 villages).

Supervisor team

There was a supervisor team in each province, and each team was comprised of three members including a health staff from PINT and two health staff from the Provincial Control Disease Center. They mornitored in the study area in indicated province.

Village collaborator

Village collaborators were in charge of sending invitation card to select households in villages based on the random household list. The selected households were informed in advance and asked to come to the designated place on the date of survey.

3.3.4. Conceptional framework

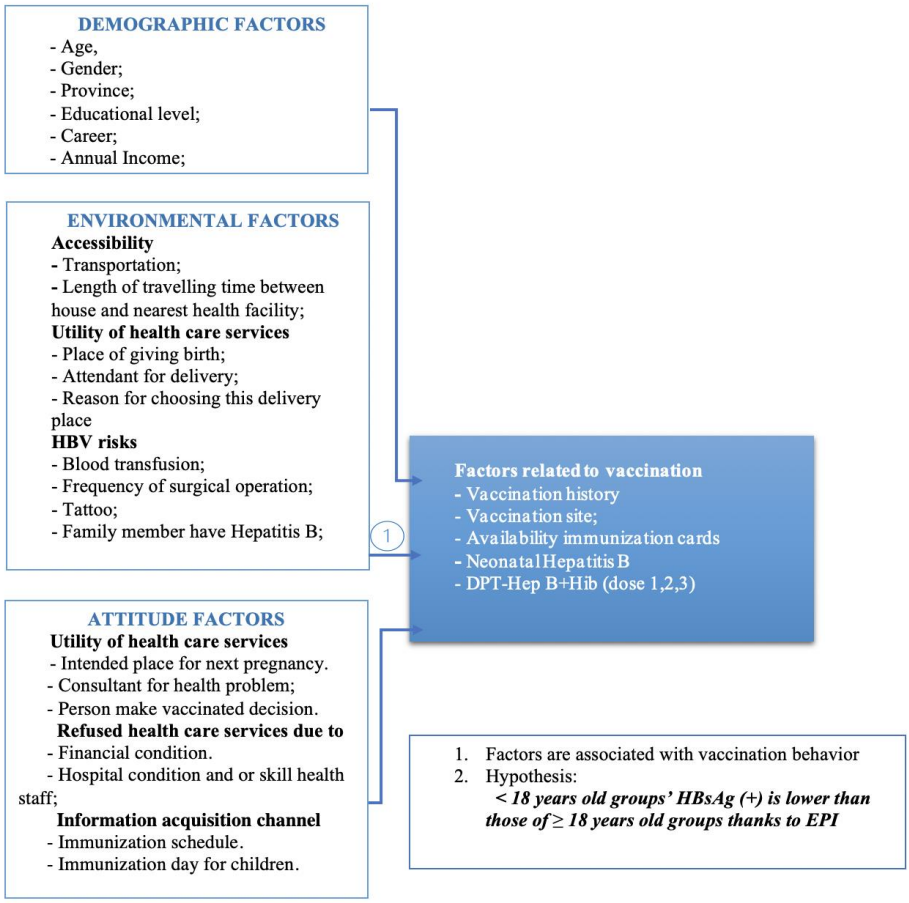


Figure 5. Conceptual Framework

3.3.5. Variables and quantification

3.3.5.1. Demographic and socio-economic factors

For every participants

- Age: divided into 2 age-groups (<18 years old and ≥ 18 years old)

- Gender: divided into 2 groups (female and male)

- Province: divided into 4 groups (Khanh Hoa, Ninh Thuan, Binh Dinh, Quang Ngai)

- Length of traveling time between house and health center: divided into 4 groups (<15 minutes; ≥15 minutes- <30minutes; ≥30 minutes)

- Transportation (using for go to healthcare center) divided into 5 groups (walking on foot, by bicycle, by motorbike, by car, others)

- Place of giving birth: divided into 7 groups (Hospital; Health center; Health station; Private clinical; House; Paddy Field, Garden, farm; Others)

- Attendant for delivery: divided into 6 groups (Medical staff; Village health volunteer; Traditional Birth Attendant; Family member & Relatives; By mother herself; Others)

- Reason for choosing this delivery place: opening question

- Vaccination history: divided into 3 groups (Yes, No, Unknown)

- Vaccination site: divided into 5 groups (Hospital, Health center, Health station, Outreach of commune site, Private doctor, Others)

- Availability of immunization card: divided into 2 groups (Yes, No)

For ≥ 18 years old participants

- Educational level: divided into 3 groups (Low (None; Primary school; Junior high school); Medium (High school); High (College /university or above; Others))

- Career: divided into 8 groups (Government and Public officer; Farmer/Fisher; Labor/work for factory; Housework, Freelancer; Company worker; Merchant; Others)

- Individual income: divided into 4 groups (>50.000.000 vnd; <50.000.000 vnd & >25.000.000 vnd; <25.000.000 vnd; Not prefer to answer)

- Way to approaching immunization schedule: divided into 10 groups (Medical staff; Village health volunteer; Vaccination bulletin; Brothers/sisters or friends; Radio / TV; Poster; Village head man/ Unit village head; Women's union told you; Others; Unknown)

- Person make vaccination decision: divided into 6 groups (Father; Mother; Both mother and father; Grandfather/ grandmother; Village head man; Others)

- Way to approaching immunization day for your children: divided into 11 groups (Medical staff; Village health volunteer; Immunization card; Brothers/sisters or friends; Radio / TV; Poster; Local authority; Women's union; Megaphone; Invitation from district manager; Others)

- Intended place for next pregnancy: divided into 7 groups (Hospital; Health center; Health station; Private clinic; House; Farm, garden and forest; Other place)

- Consultant for health problem: divided into 7 groups (Husband/wife; Other family members; Medical staff; Village health volunteer; Local authority; Friends / neighbors; Other)

- Refusing health care service due to financial condition: divided into 3 groups (Yes, No, No health problem)

- Health care service refusing due to financial condition: divided into 9 groups (Maternal and childcare; Immunization; Malaria; Tuberculosis; Hypertension; Diabetes; Cancer; Rehabilitation; Others)

- Refusing health care service due to hospital condition and or skill health staff: divided into 3 groups (Yes, No, No health problem)

- Health care service refusing due to hospital condition and or skill health staff: divided into 9 groups (Maternal and childcare; Immunization; Malaria; Tuberculosis; Hypertension; Diabetes; Cancer; Rehabilitation; Others)

- Blood transfusion: divided into 3 groups (Yes, No, Unknown)

- Tatoo: divided into 2 groups (Yes, No)

- Frequency of surgical operation: divided into 4 groups (Never, Once, Twice or more; Unknown)

- Family member have Hepatitis B: divided into 3 groups (Yes, No, Unknown)

3.3.5.2. Vaccination history

- Neonatal Hepatitis B dose (0-24hours)

- DPT-Hep B+Hib (dose 1,2,3)

3.4. ANALYTICAL METHODS

- The data was checked before entry in Excel. Data entry for HBsAg and questionnaire will be conducted in the PINT. Brief analysis was done in NCGM and discussed among PINT, NCGM.

- Data processing is coded, and statistic by SPSS 25.0.

- The categorical data was reported as number and percentage.

- Data analysis was undertaken using chi square tests and multiple logistic regression model.

3.5. ETHICS STUDY

Study conducted collecting primary data underwent an IRB approval and ethical review with the research proposal from PINT, NCGM. Secondary data is used in this thesis after receiving approval from ethical Council of Yonsei University Health System, under the agreement of PINT and NCGM.

Participants are asked to sign on the consent form after informing them of the freedom of decline and other rights in a non-coercive environment.

If participants are less than 18 years old, the consents are obtained from their parents or caregivers.

Dataset that involves the individual name (anonymous), address and other results including serological status was be kept strictly confidential. The dataset is totally prompt.

CHAPTER 4

RESULTS

4.1. DEMOGRAPHIC CHARACTERISTICS OF RESEARCH PARTICIPANTS IN CENTRAL REGION OF VIETNAM

Table 1: General demographic characteristics of research participants in Central region of Vietnam

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)			Total (any age) (n=2075)		
	Total	HBsAg(+)		Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%		N	%
Mean of Age (Mean ± SD)	29.66 ± 6.107			8.87±4.726			18.45± 11.69		
Gender									
Male	253	29	11.46%	553	10	1.81%	806	39	4.83%
Female	703	58	8.25%	566	15	2.65%	1269	73	5.75%
Province									
Khanh Hoa	278	25	8.99%	255	5	1.96%	533	30	5.62%
Ninh Thuan	256	30	11.72%	270	5	1.85%	526	35	6.65%
Quang Ngai	226	16	7.08%	297	7	2.36%	523	23	4.4%
Binh Dinh	196	16	8.16%	297	8	2.69%	493	24	4.87%
Level of Education									
Low	520	46	8.85%	-	-		-	-	
Medium	237	24	10.13%	-	-		-	-	
High	181	17	9.39%	-	-		-	-	
Others	18	0	0	-	-		-	-	
Occupation									
Government & Public officer	123	13	10.57%	-	-		-	-	

Farmer / Fisherman	344	33	9.59%	-	-		-	-	
Labor/work for factory	60	7	11.67%	-	-		-	-	
Company worker	20	1	5.00%	-	-		-	-	
Merchant	107	10	9.35%	-	-		-	-	
Housework	106	10	9.43%	-	-		-	-	
Freelancer	77	2	2.60%	-	-		-	-	
Others	119	11	9.24%	-	-		-	-	
Annual Income									
≥50.000.000 vnd	230	24	10.43%	-	-		-	-	
< 50.000.000 vnd & ≥25.000.000 vnd	190	16	8.42%	-	-		-	-	
<25.000.000 vnd	198	16	8.08%	-	-		-	-	
Not prefer to answer	338	31	9.17%	-	-		-	-	

(-): not applicable

The number of participants in the survey was 2,075 participants, which were divided into 2 age groups: ≥ 18 years old (n= 956; 46.1%) and <18 years old (n= 1119; 53.9%). The number of females was higher than males in group ≥ 18 years old, and this figure was equal in the group <18 years old. The total proportion of HBsAg (+) was (n=112; ~ 5.4%), in which the ≥ 18 years old (9.1%) and <18 years old (2.23%). This figure of male was well- above higher than female, at 11.46% and 8.25% respectively in group ≥ 18 years old; but this figure was reversely with male: 1.18% and female: 2.65% respectively in group <18 years old.

The sample of participants distributed quite similarly in 4 selected provinces. Ninh Thuan province reached the highest positive HBsAg(+) cases (group ≥ 18 years old :11.72%; group <18 years old: 1.85%) out of 4 selected provinces at two age-groups, followed by Khanh Hoa and Binh Dinh with a quite similar proportion of HBsAg(+) in two age groups (group ≥ 18 years old :8.99%; group <18 years old: 1.96%); (group ≥ 18 years

old :8.16%; group <18 years old: 2.69%) respectively. Quang Ngai shared the smallest proportion of HBsAg (+), around (group ≥ 18 years old: 7.08%; group <18 years old: 2.36%).

Most of participants ≥ 18 years old had low level of education, though the highest HbsAg (+) percentage was the most prominent in medium education level (high school) (n= 24;10.13%), high level education (college and above) (n=17; 9.39%), low level of education (none, primary school and junior high school) (n=46; 8.85%) and others was not significant.

The popular career in selected participants were farmer/fisherman (35.9%); government and public officer (12.9%); merchant (11.2%); housework (11.1%). The prevalence of HBsAg (+) was the most prominent in labor/work for factory (n=7;11.67%), followed by the government and public officer (n=13; 10.57%), the proportion of HBsAg (+) from others popular sectors such as farmer/fisherman, merchant, housework tied at roughly in the range from 9.24-9.59%; lower cases in groups of company worker (n=1,5%) and freelancer (n=2, 2.6%).

On average, the annual income for each household are range from under 25 million VND to over 50 million VND and there was no big gap percentage difference participants among those groups (≥50.000.000 vnd: 24%; < 50.000.000 vnd & ≥25.000.000 vnd:19.87%; <25.000.000 vnd: 20.7%). However, the number of people not prefer to answer was quite high (33.2%). The significant HBsAg (+) percentage ≥50.000.000 vnd group (n=24; 10.43%), followed by the groups had no respond, while the percentage of other groups were quite similar (<50.000.00 and ≥25.000.000 vnd n= 16; 8.42%; <25.000.000 vnd: n= 16; 8.08%).

4.2. ENVIRONMENTAL FACTORS AFFECT TO USING HEALTH CARE SERVICES OF PARTICIPANTS IN CENTRAL REGION, VIETNAM

Table 2: Percentage of HBsAg (+) according to the accessibility to health facility

Variables	≥18 years old (n= 956)			< 18 years old (n= 1119)			Total (any age) (n=2075)		
	Total	HBsAg(+)		Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%		N	%
Main transportation to the nearest health facility									
On foot	65	5	7.69%	85	5	5.88%	150	10	6.67%
Bicycle	31	0	0	66	0	0	97	0	0
Motorbike	852	82	9.62%	954	20	2.10%	1806	102	5.65%
Car	5	0	0	4	0	0	9	0	0
Others	3	0	0	10	0	0	13	0	0
Time to nearest health facility									
<15 minutes	869	80	9.21%	996	22	2.21%	1865	102	5.47%
≥15 minutes-<30minutes	49	3	6.12%	90	1	1.11%	139	4	2.88%
≥30 minutes	38	4	10.53%	33	2	6.06%	71	6	8.45%

(-): not applicable

Residents tend to use the motorbike (87.04%) as a priority transportation to approach the nearest health facility, the second way was go on foot (7.2%). The other vehicle (bicycle, car, electric bicycle) was not popular use. The prevalence of HBsAg (+) was highest in group using motorbike (≥ 18 years old: n=82; 9.62% and <18 years old n= 20; 2.1% and in on foot group this prevalence (≥ 18 years old: n=5; 7.69 %) and <18 years old (n= 5; 5.88%), other groups has no positive cases.

The distance between their house and health facility taking mostly under 15 minutes accounts for the highest proportion (88.9%), though the highest proportion of

HBsAg (+) in both age groups in the participants approach to health facilities over 30 minutes (≥ 18 years old: n=4, 10.53%) and <18 years old: n=2, 6.6%).

Table 3: Percentage of HBsAg (+) according to the health services

Variables	≥18 years old (n= 956)			< 18 years old (n= 1119)			Total (any age) (n=2075)		
	Total	HBsAg(+)		Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%		N	%
Place of giving birth									
Hospital	297	26	8.75%	755	11	1.46%	1052	37	3.52%
Health center	78	6	7.69%	121	1	0.83%	199	7	3.52%
Health station	181	16	8.84%	89	5	5.62%	270	21	7.78%
Private clinical	12	1	8.33%	27	0	0	39	1	2.56%
House	351	37	10.54%	125	7	5.60%	476	44	9.24%
Paddy Field, Garden, farm	0	0	-	0	0	-	0	0	-
Others	37	1	2.70%	2	1	50.00%	39	2	5.13%
Attendant for delivery									
Medical staff	572	52	9.09%	987	16	1.62%	1559	68	4.36%
Village health volunteer	6	0	0	7	0	0	13	0	0
Traditional Birth Attendant	281	26	9.25%	89	7	7.87%	370	33	8.92%
Family member & Relatives	103	13	12.62%	72	3	4.17%	175	16	9.14%
By mother herself	9	1	11.11%	0	0	-	9	1	11.11%
Others (unknown)	46	3	6.52%	4	1	25.00%	50	7	14%
Reason for choosing this delivery place									
Complicated case	21	4	19.05%	114	2	1.75%	135	6	4.44%
Convenience	218	21	9.63%	185	3	1.62%	403	24	5.96%

Effortless delivery	26	2	7.69%	34	1	2.94%	60	3	5%
Financial and external condition	97	13	13.40%	42	4	9.52%	139	17	12.23%
Individual selection	101	14	13.86%	68	4	5.88%	169	18	10.65%
Mother and child safety	253	20	7.91%	555	7	1.26%	808	27	3.34%
Quality administrative & experts	68	4	5.88%	86	1	1.16%	154	5	3.25%
Unknown	172	9	5.23%	35	3	8.57%	205	12	5.85%

Using health facilities for delivery was the top noteworthy considered option for both age-groups (hospital: 50.3%, health station: 13%, health center: 9.6%), while the percentage of having birth at home still existed (22.9%). The prevalence of HBsAg (+) was dramatical evaluated in ≥ 18 years old group comparing to the <18 years old group, which the highest in delivery in house in ≥ 18 years old group (≥ 18 years old: n=37, 10.54 % and <18 years old: n=7; 5.6%), followed by health station (≥ 18 years old: n=16, 8.84 % and <18 years old n= 5; 5.62%), and hospital (≥ 18 years old: n=26, 8.75 %) and <18 years old: n=11; 1.46%).

Most of attendant for delivery for both age-groups are health staff such as medical staff (75.2%); traditional birth attendant (17.8%) and family members & relatives (8.4%). However, the prevalence of HBsAg (+) in family members & relatives sector (≥ 18 years old: n=13; 12.62% and <18 years old: n=3; 4.17%) was the highest, then mother herself sector (≥ 18 years old: n=1; 11.11%); group having traditional birth attendant (≥ 18 years old: n=26; 9.25%) and <18 years old n=7; 7.87%), medical staff attendant (≥ 18 years old: n=52; 9.09%) and <18 years old: n=16; 1.62%).

Convenience (≥ 18 years old: n=218 and <18 years old: n=185) and Mother and child safety (≥ 18 years old: n=253 and <18 years old: n=555) were the frequently choice

for delivery places in both age-groups. In complicated case sectors, the prevalence of HBsAg (+) in ≥ 18 years old age-group was the highest (n=4; 19.05%). Financial and external condition considered as an relevant reason to delivery place decision in both age groups, which was one of those sectors had high prevalence of HBsAg (+) (≥ 18 years old: n=97, HBsAg (+): n=13, 13.4%) and <18 years old n=42; HBsAg (+): n=4, 9.52%).

Table 4:Percentage of HBsAg (+) according to the Hepatitis B infection risks

Variables	≥18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Blood transfusion						
Yes	45	9	20.00%	-	-	
No	880	78	8.86%	-	-	
Do not know	31	0	0	-	-	
Tattoo						
Yes	59	4	6.78%	-	-	
No	897	83	9.25%	-	-	
Frequency of surgical operation						
Never	682	62	9.09%	-	-	
Once	164	15	9.15%	-	-	
Twice or more	85	9	10.59%	-	-	
Do not know	25	1	4.00%	-	-	
Family member have Hepatitis B						
Yes	92	28	30.43%	-	-	
No	642	36	5.61%	-	-	
Do not know	222	23	10.36%	-	-	

(-): no applicable

Blood transfusion did not exist in many ≥ 18 years old participants (n=880; 92.5%), though the prevalence of HBsAg (+) in group having blood transfusion was higher 2.26 times comparing to group having no blood transfusion. Reversely, it shares the different trend as ≥ 18 years old participants group having no tattoo with (n=897; 93.8%) but its prevalence of HBsAg (+) was higher comparing to group having tattoo (9.25%, 6.78% respectively).

The proportion of population never has surgical operation (n=682; 71.6%). The prevalence of HBsAg (+) was higher progressively as the increasing of the number of surgical operation times (never: n=62; 9.09%; once: n=15; 9.15%; twice or more: n= 9; 10.59%).

Mostly, people had no family members having Hepatitis B and the prevalence of HBsAg (+) was the higher in participants group having Hepatitis B (n=28; 30.43%), as 5.4 times comparing to the group have no Hepatitis B (n=36; 5.61%), However, the positive status of HBV infection in group do not know their family status was significantly (n=23; 10.36%).

Table 5:Percentage of HBsAg (+) according to the vaccination behaviors

Variables	≥18 years old (n= 956)			< 18 years old (n= 1119)			Total (any age) (n=2075)		
	Total	HBsAg(+)		Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%		N	%
Vaccination history									
Yes	634	50	7.89%	1066	23	2.16%	1700	73	4.29%
No	212	32	15.09%	20	2	10.00%	232	34	14.66%
Unknown	110	5	4.55%	33	0	0	143	5	3.50%
Vaccination site									
Hospital	32	2	6.25%	144	1	0.69%	176	3	1.70%
Health center	50	6	12.00%	46	1	2.17%	96	7	7.29%

Health station	552	44	7.97%	981	21	2.14%	1533	65	4.24%
Outreach of commune site	42	2	4.76%	50	2	4.00%	92	4	4.35%
Private doctor/clinic	16	1	6.25%	5	0	0	21	1	4.76%
Others	17	1	5.88%	4	0	0	21	1	4.76%
Availability of immunization cards									
Yes	5	0	0	285	6	2.11%	290	6	2.07%
No	951	87	9.15%	834	19	2.28%	1785	106	5.94%

(-): not applicable

In both age-groups, most of participants have historical of vaccination. The prevalence of HBsAg (+) in participants have no historical vaccination in group ≥18 years old (n=32, 15.09%) was higher than group <18 years old(n=2,10%); and this prevalence was higher as well above twice comparing to group having historical of vaccination (≥ 18 years old: n=50, 7.89%; <18 years old: n=23, 2.16%).

Health station was the most popular place for vaccination out of options (73.1%), followed with hospital (8.5%) for both age groups. The prevalence of HBsAg (+) in health center was the highest (≥ 18 years old: n=6, 12%); <18 years old: n=1, 2.17%); but the second position was in health station (≥ 18 years old: n=44, 7.97%; <18 years old: n=21, 2.14%); hospital had the proportion of positive cases (≥ 18 years old: 2, 6.25%; <18 years old: n=1, 0.69%).

The numerous absence of their immunization card (86.7%) in both age-groups, which the prevalence of HBsAg (+) in this group was (≥ 18 years old: n=87, 9.15%; 9 times higher compare to group having immunization card; <18 years old:n=19, 2.28%; quite equal to group having immunization card(n=6;2.11%)).

Table 6: Hepatitis B doses distribution among participants from 12-48 months old in Central Region Vietnam.

Variables	12-48 months old (n= 264)								
	Proper time immunization			Improper time immunization			No immunization		
	Total	HBsAg(+)		Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%		N	%
Hepatitis B dose 0 (Birth dose)	96	1	1.04%	17	0	0	151	3	1.99%
Hepatitis B dose 1	70	1	1.43%	97	2	2.06%	98	1	1.02%
Hepatitis B dose 2	132	2	1.52%	32	1	3.13%	100	1	1%
Hepatitis B dose 3	109	1	0.92%	53	2	3.77%	102	1	0.98%

Proper time immunization doses tended to increase, especially in Hepatitis B dose 2 (n=132, 50%) and Hep 3 (n=109, 41.28%). However, the number of those having no immunization is still high dramatically, range from 37-57%. The prevalence of HBsAg (+) was increasing gradually in improper time immunization group (0%-3.77%) and remained quite steady in both groups: proper time immunization (0.92%-1.52%) and no immunization (0.98%- 1.99%) respectively.

The number of infants having vaccination was low, at n=96, 36.3%. The prevalence of HBsAg(+) of children having birth dose accounted for 1.04%, which was lower than those did not have birth dose, at 1.99%. Among 4 Hepatitis B doses, Hepatitis B dose 1 got lowest proportion in 2 sectors: proper time immunization (26.5%); no immunization (37.1%) but highest in improper time immunization sector (36.7%). Hepatitis B dose 2 and Hepatitis B dose 3 shared the resemblance trend of growing proper time immunization doses, though group of having no vaccination group with high proportion.

Table 7: Prevalence of HBsAg (+) according to vaccination status among 12-48 months old infants and toddlers in Central Region Vietnam.

Variables	12-48 months old (n= 264)		
	Total	HBsAg(+)	
		N	%
Adequate and proper time	28	0	0
Inadequate and (or) improper time	137	3	2.19%
No vaccination	99	1	1.01%

There had no HBsAg (+) among 28 children having adequate and proper time. There were 3 cases with HBsAg (+) in improper time and (or) inadequate vaccination group (2.19%) and this figure in group with no vaccination at 1.01%.

4.3. ATTITUDE FACTORS AFFECTS TO USING HEALTH CARE SERVICES OF PARTICIPANTS IN CENTRAL REGION, VIETNAM

Table 8: Percentage of HBsAg (+) according to the intended delivery place for next pregnancy and consultant for health problem.

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Intended place for next pregnancy						
Hospital	539	51	9.46%	-	-	
Health center	38	2	5.26%	-	-	
Health station	72	7	9.72%	-	-	
Private clinic	2	0	0	-	-	
House	27	3	11.11%	-	-	
Farm, garden and forest	0	0	-	-	-	
Other places	278	24	8.63%	-	-	

Single	32	2	6.25%	-	-	
No Intention	193	19	9.84%	-	-	
Unknown	53	3	5.66%	-	-	
Consultant for health problem						
Husband/wife	168	19	11.31%	-	-	
Other family members	227	22	9.69%	-	-	
Medical staff	726	69	9.50%	-	-	
Village health volunteer	30	2	6.67%	-	-	
Local authority	4	1	25.00%	-	-	
Friends / neighbors	30	3	10.00%	-	-	
Others	107	11	10.28%	-	-	

(-): not applicable

Most people choose health facilities for their/ their wife next pregnant, in which the prominent choice go for hospital with 56.33%; health station was the second selection out of places (7.53%) and health center (3.97%). The prevalence of HBsAg (+) in group choosing hospital (51; 9.46%) and house (n=3, 11.11%).

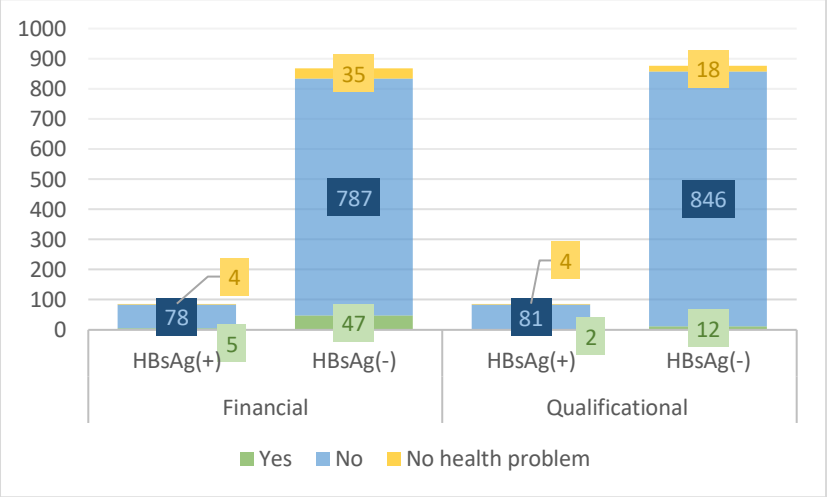
Population usually come to medical staff for asking consultant (n=726, 75.9%) with lofty HBsAg (+) (n=69,9.5%), though this figure for partner (n=168, 17.6%; HBsAg(+):n=19,11.31%) and other family members (n=227, 23.7%; HBsAg(+): n=22, 9.69%) and friend (n=30, 3.14%; HBsAg(+): n=3, 10%) are also admired.

Table 9: Percentage of HBsAg (+) according to the reasons for refusing health care services

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Refusing health care services due to the financial condition						
Yes	52	5	9.61%	-	-	
No	865	78	9.01%	-	-	
No health problem	39	4	10.26%	-	-	

Refusing health care services due to the hospital condition or skill health staff						
Yes	14	2	16.67%	-	-	
No	921	81	9.64%	-	-	
No health problem	21	4	23.5%	-	-	

Figure 6. Reasons for refusing health care services



F: Financial, Q: Qualification

Most of participant have no problem of access health services in light of financial condition (n=865, 90.48%) and quality condition (n=921, 96.3%). The number of participants who refused to use health services were quite small in both above groups. The prevalence of HBsAg (+) was highest in group without health problem (F:10.26%; Q:23.5%), though the prevalence of positive cases in the group with no refusing health services. (F:9.01%; Q: 9.64%) and refusing health services (F: 9.61%; Q:16.67%).

Table 10: Percentage of HbsAg (+) according to the common diseases are refused by financial (F) and qualification (Q) condition

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Categories of health care services refusing due to financial condition						
Maternal and childcare	3	0	0	-	-	
Immunization	2	0	0	-	-	
Malaria	2	0	0	-	-	
Tuberculosis	0	0	-	-	-	
Hypertension	1	0	0	-	-	
Diabetes	6	0	0	-	-	
Cancer	9	2	22.2%	-	-	
Rehabilitation	3	0	0	-	-	
Others	30	1	3.3%	-	-	
Categories of health care services refusing due to its qualification						
Maternal and childcare	0	0	0	-	-	
Immunization	1	0	0	-	-	
Malaria	0	0	-	-	-	
Tuberculosis	0	0	-	-	-	
Hypertension	1	0	0	-	-	
Diabetes	1	0	0	-	-	
Cancer	3	1	33.3%	-	-	
Rehabilitation	0	0	-	-	-	
Others	8	1	12.5%	-	-	

Apart from mentioned diseases, cancer was the most popular disease (0.93%; 0.3%) with the highest HBsAg (+) F:22%; Q: 33% respectively. Other diseases were mostly minor positive HBsAg (+) cases.

Table 11:Percentage of HbsAg (+) according to the information acquisition channel about immunization schedule and immunization day for children of participants in Central region, Vietnam

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Information acquisition channel about immunization schedule						
Medical staff	600	58	9.67%	-	-	
Village health volunteer	445	36	8.1%	-	-	
Immunization card	112	11	9.82%	-	-	
Brothers/sisters or friends	15	2	13.3%	-	-	
Radio / TV	66	9	13.64%	-	-	
Poster	14	1	7.14%	-	-	
Village head man/Unit village head	107	11	10.28%	-	-	
Women's union	103	10	9.7%	-	-	
Others	5	0	0	-	-	
Unknown	174	13	7.47%	-	-	
Information acquisition channel about immunization day for your children						
Medical staff	448	40	8.93%	-	-	
Village health volunteer	286	20	6.99%	-	-	
Vaccination card	17	3	17.65%	-	-	
Brother/ sister/ friend	38	4	10.53%	-	-	
Radio/ TV	8	1	12.50%	-	-	
Poster	70	8	11.43%	-	-	
Local authority	106	11	10.38%	-	-	

Woman's union	106	13	12.26%	-	-	
Megaphone	5	1	20%	-	-	
Invitation from the district governor	159	12	7.55%	-	-	
Others	797	75	9.41%	-	-	

Information acquisition channel about immunization schedule and immunization day for children from medical staff (n=600, 62.8%; n=448, 46.9% respectively), village health volunteer (n=445,46.5%; n=286, 29,9% respectively), immunization card (n=112; 12.65%, n=17; 1.78% respectively).

The prevalence of HBsAg (+) was the most prominent in receiving this information from media (radio, internet, TV) (immunization schedule 13.64%) and immunization card (immunization day for children: 17.65%), followed by getting from friends/ family members (immunization schedule 13.3%; immunization day for children: 10.53%).

Table 12: Percentage of HbsAg(+) according to the person who make vaccinated decision

Variables	≥ 18 years old (n= 956)			< 18 years old (n= 1119)		
	Total	HBsAg(+)		Total	HBsAg(+)	
		N	%		N	%
Person make vaccinated decision						
Father	64	5	7.81%	-	-	
Mother	466	41	8.80%	-	-	
Both mother and father	274	29	10.58%	-	-	
Grandfather/ grandmother	1	0	0	-	-	
Village head man	151	12	7.95%	-	-	
Other	805	75	9.32%	-	-	

The number of mothers who take responsibility for making vaccinated decision were 468 out of 924 participants (48.7%). The prevalence of HBsAg (+) in mother sector (n=41, 8.8%); both mother and father (n=29, 10.58%) while grandparents' sector do not have any case. Besides, the others sector (single) was significant attention among sector with the high prevalence of HBsAg (+) (n=75, 9.32%).

4.2. ASSOCIATION BETWEEN SEVERAL FACTORS AND PREVALENCE OF HBSAG POSITIVE IN CENTRAL REGION, VIETNAM

Table 13: Logistic regression analysis of several factors related to prevalence of HBsAg positivity in Central region, Vietnam

Variables	HBsAg(+)		
	OR	95% CI	p-value
Age group			
≥ 18 years old*	1.0	-	-
<18 years old	0.228	0.145-0.359	**p<0.001[a]**
Reason to choose delivery place			
Complicated case*	1.0	-	-
Convenience	0.756	0.277-2.065	
Effortless delivery	1.029	0.504-2.102	
Financial and external condition	0.855	0.233-3.135	
Individual selection	2.264	1.045-4.904	**p<0.05[a]**
Mother and child safety	1.937	0.905-4.145	
Quality administrative & experts	0.562	0.280-1.129	
Unknown	0.545	0.188-1.582	
Any family member has Hepatitis B			
Yes*	1.0	-	-
No	3.861	2.079- 7.171	**p<0.001[a]**
Unknown	0.518	0.30- 0.895	**p<0.05[a]**
Vaccination history			

Yes*	1.0	-	-
No	1.238	0.492-3.115	
Unknown	4.739	1.808-12.422	**p<0.05[a]**
Availability of immunization cards			
Yes*	1.0	-	-
No	2.988	1.300-6.867	**p<0.05[a]**

(*): reference group; (-): no applicable

a: Logistic regression model

After adjusting for other factors, logistic regression model gives the following results:

- The proportion of participants in age group under 18 years old having lower chance to get HBsAg (+) 0.228 times, compared to the age group ≥ 18 years old.
- The proportion of participants having their own individual selection getting HBsAg (+) was higher than complicated case sector, at 2.264 times.
- The proportion of participants did not have and did not know their family member status of Hepatitis B having chance to get HBsAg (+) was higher 3.861 times and lower 0.518 times respectively, compared to the group of participants known their family member status.
- The proportion of participants did not know their vaccination history getting HBsAg (+) was higher than those who have vaccinated before, at 4.739 times.
- The proportion of participants having no immunization card getting HBsAg (+) was higher than those who had immunization card, at 2.988 times.

Variables	HBsAg(+)			
	OR	95% CI	p-value	
Attendance for delivery				
Medical staff				
No*	1.0	-	-	
Yes	0.489	0.330-0.725	**p<0.001[a]**	
Village health volunteer				
No*	1.0	-	-	
Yes	0.000	0.000- .	p>0.05	
Traditional Birth Attendant				
No*	1.0	-	-	
Yes	2.015	1.321-3.076	**p=0.001[a]**	p>0.05
Family member & Relatives				
No*	1.0	-	-	
Yes	1.891	1.087-3.289	**p<0.05[a]**	
By mother herself				
No*	1.0	-	-	
Yes	0.000	0.000- .	p>0.05	
Others (unknown)				
No*	1.0	-	-	
Yes	1.543	0.546-4.367	p>0.05	

(*): reference group; (-): no applicable

a: Logistic regression model

Note: Only relevant variables with statistical significance (p <0.05) in the logistic regression analysis is presented in the table above.

After adjusting for other factors, logistic regression model gives the following results:

- There was an association between the prevalence of HBsAg (+) to people who attend to participants' delivery in their birth delivery/ their wife's birth delivery:

+ The group of participants who had attend of medical staff has lower chance of getting HBsAg(+) comparing to those did not have this attendant, at 0.489 times.

+ The group of participants who had attend of traditional birth attendant has higher chance of getting HBsAg(+) comparing to those did not have this attendant, at 2.015 times.

+ The group of participants who had attend of family member & relatives has higher chance of getting HBsAg(+) comparing to those did not have this attendant, at 1.891 times.

CHAPTER 5
DISCUSSION

5.1. DEMOGRAPHIC CHARACTERISTICS OF RESEARCH PARTICIPANTS IN THE CENTRAL REGION OF VIETNAM

As of appropriate 2,075 samples were selected in 4 provinces including Khanh Hoa, Ninh Thuan, Quang Ngai and Binh Dinh, which were divided into 2 age groups: ≥ 18 years old: n= 956, 46.1%) and <18 years old: n=1119, 53.9%).

5.1.1. Age, gender and location

The decline in the prevalence of HBsAg in younger age groups may be attributed to the immunization program. Peng Huang et al presented the same trend of prevalence of HBsAg(+) was low in children (0.7-0.77%), and gradually increasing in the adolescent (1.4-2.55%) and adult aged ≥ 20 years old (5.69-11.22%)[83]. Susan T et al also indicated the risk of age and the prevalence of HBsAg (+) dependent in childhood and adult period in her study about estimate global HBV disease burden and vaccination impact acute HBV, indicated the prevalence of HBsAg(+) acute infected occur in ~1% perinatal, 10% early childhood and 30% of late infections, while the spread out of chronic HBV occur in ~90% of persons infected in perinatally, 30% infected in early childhood, and 6% in effected after 5 years of age. Therefore, it can explain for the risk of getting higher prevalence of HBsAg(+) in 18 years old and above age-group[7].

The number of participants in survey were equal in 4 provinces and Ninh Thuan got the highest proportion of HBsAg (+) in group ≥ 18 years old :11.72%; group <18 years old: 1.85% . Son Do et al conducted in 509 participants above 20 years old about Hepatitis B&C among adults living in Binh Thuan province, Vietnam, showing the prevalence of HBsAg(+) among participants was 15.3% (95% CI, 12.2-18.5%) higher than our study results[84]. The amount of female percentage was higher than male in ≥ 18 age-group (73.53%, 26.43% respectively) and this figure was equal in <18 years old age-group (50.58%, 49.35% respectively). The incidence of HBsAg (+) in survey was 112 cases,

accounts for ~5.4%, the number of positive cases was mostly in male as approximately one and a half as female at 11.46% and 8.25% respectively in group ≥ 18 years old; but this figure was reversely with male: 1.18% and female: 2.65% respectively in group <18 years old. Possible hypothesis can explain by the rapid test used in this study has a reported sensitivity of 95%; therefore, the HBsAg prevalence in this study might be lower than the true seroprevalence. Plus, the overlapped the time of interview to the harvest time, so most of mother will take their children to interview days. Besides, the random collection samples may get the proportion of female higher (1269 samples).

5.1.2. Levels of education

The research involved some information spending only for participants over 18 years old to identify their understand and behavior toward HBsAg(+), including 956 samples. Most of participants ≥ 18 years old have low level of education. The highest HBsAg(+) percentage was the most prominent in medium education level (high school) (24;10.13%), high level education (college and above) (17; 9.39%), low level of education (none, primary school and junior high school) (46; 8.85%) and others was not significant. Balaeva T et al shared the different progressive trend as our result in their seroprevalence of markers of Hepatitis B virus infection in 1243 adults from 18-39 years old in Arkhangelsk, Northwest Russia that the prevalence of HBsAg(+) in the low level of education was the most higher (15.8%), though this figure between medium and high education level were pretty equal (9.9%, OR: 0.59, 95% CI: 0.35-0.999) and (10%, OR: 0.59, 95% CI: 0.38-0.92)[85]. Peng Huang et al demonstrated the prevalence of HBsAg(+) in local residents of all age groups living in Jiangsu provinces, Eastern China that participants who were illiterate or had primary school diplomas had the highest HBsAg prevalence (9.82%, 95%CI: 9.60%-10.05%), followed by middle school (8.35%, 95%CI: 8.09%-8.62%) and college school groups (8.05%, 95%CI: 7.42%-8.70%)[83].

5.1.3. Occupations

The popular career in selected participants were farmer/fisherman (35.9%); government and public officer (12.9%); merchant (11.2%); housework (11.1%). The

prevalence of HBsAg (+) was the most prominent in labor/work for factory (7;11.67%), followed by the government and public officer (13; 10.57%), the others popular sectors such as farmer/fisherman, merchant, housework share quite similar proportion of HBsAg (+) in the range from 9.24-9.59%; lower cases in groups of company worker (1;5%) and freelancer (2,2.6%). Comparing to the ubiquitous levels of HBsAg (+) proportion in, mother and their children in Laos people, 2015 by Komada et al, farmer prevalence accounted for the highest figure at 64.64%, (with HBsAg (+) children 2.21%; 95% CI 1.02-3.4 and mother: 3.23%, 95% CI 1.79-4.66), though the number of fishermen was the lowest one due to their geography as a landlock country. The prevalence of HBsAg (+) in all sectors in Laos is lower to Vietnam figures. The highest proportion of HBsAg(+) in Laos people belonged to merchant (children 5.56%; 95% CI 0.00-11.87 and mother:11.11% , 95% CI 2.45-19.77), though this figure on labor sector was on second high position(3.39%)[86].

5.1.4. Income

In average, the annual income for each household are range from under 25 million VND to over 50 million VND and there was no big gap percentage difference among those groups (≥50.000.000 vnd: 24%; < 50.000.000 vnd & ≥25.000.000 vnd:19.87%; <25.000.000 vnd: 20.7%). The significant HbsAg (+) percentage ≥50.000.000 vnd group (24; 10.43%), followed by the groups have no respond, while the percentage of other groups are quite similar (<50.000.00 and ≥25.000.000 vnd 16; 8.42%; <25.000.000 vnd: 16; 8.08%). Balaeva. T et al conducted in 1243 adults from 18-39 years old in Arkhangelsk, Northwest Russia, 2010-2011 showed the participants with low income has higher serological marker of HBV, with low, medium and high income are 15.5%, 10.1%, 9.9% respectively[85]. Jindai N et al determine the prevalence of sexual transmitted infections, including Hepatitis B among 500 pregnant women, which demonstrates the elevated of HBsAg (+) in group having low and upper socioeconomic status are equally (2.7%)[87]. Comparing to other studies, we present adverse results with the positive HBsAg are highest in wealthy sector and lowest in low-income sector. Possible hypothesis can explain for this

reason related to society issue (unsafety sexual behavior of husbands, history of STIs in their partners, or no re-vaccination for a long time, especially in adults). Besides the number of people do not prefer to answer was quite high (33.2%) with the significant HBsAg (+) percentage (31; 9.17%), even higher than the ≥50.000.000 vnd sector, it was very difficult to identify the relevance of affection of income and HBsAg (+) prevalence.

5.2. ENVIRONMENTAL FACTORS AFFECT TO USING HEALTH CARE SERVICES OF PARTICIPANTS IN CENTRAL REGION, VIETNAM

5.2.1. Accessibility to health facility

5.2.1.1. Main transportation to the nearest health facility

Participants tend to use the motorbike (87.04%) as a priority transportation to approach the nnearesthealth facility, the second way was going on foot (7.2%). The other vehicle (bicycle, car, electric bicycle) are not popular use. The prevalence of HBsAg(+) was highest in group using motorbike (≥ 18 years old (n=82; 9.62%) and <18 years old (n= 20; 2.1%) and in on foot sector, this prevalence (≥ 18 years old: =5; 7.69 %) and <18 years old (n= 5; 5.88%), others groups has no positive cases. Komada et al studied on 911 mother and their children in Laos, 2015 showed the main transportation to the nearest health facility much more variety (bicycle, car, hand tractor, on foot,…) than our result, though motorbike was the most popular vehicle (554; 61.15%) and this belonged participants in this sector presented the highest number of HBsAg(+) cases in both mother (21, 3.79%, 95% CI: 2.20-5.39) and their child (15; 2.71%, 95% CI: 1.35-4.06)[86].

5.2.1.2. Time to nearest health facility

The distance between their house and health facility taking mostly under 15 minutes accounts for the highest proportion (88.9%), though the highest proportion of HBsAg (+) in both age groups in the participants approach to health facilities over 30 minutes (≥ 18 years old: 4; 10.53%) and <18 years old: 2; 6.6%). It is predicted by the difficult approach to the health facilities, which makes population could not have early diagnosis. Reversely, the amount of time of moving from house to nearest facility in Laos

was the most prominent in range from > 10minutes to ≤30 minutes by Komada et al, though the prevalence of HBsAg(+) were highest in ≤10 minutes sector in both mother (10; 5.75%, 95% CI: 2.25-9.24) and their child (8, 4.6%, 95% CI: 1.45-7.74)[86].

5.2.2. Health services

5.2.2.1. Place of giving birth

Using health facilities for delivery was the top noteworthy considered option (hospital: 50.3%, health station: 13%, health center: 9.6%), while the percentage of having birth at home still existed (22.9%). The prevalence of HBsAg (+) was highest in delivery in house (≥ 18 years old: n=37, 10.54 % and <18 years old: n= 7; 5.6%), followed by health station (≥ 18 years old: n= 16, 8.84 % and <18 years old n=5; 5.62%), and hospital (≥ 18 years old: n=26, 8.75 %) and <18 years old: n=11; 1.46%). At home, participants do not have adequate and hygiene medical equipment, hence, the risk of getting HBsAg (+) was very transparent high. We share the homogeneous trend of Hien Nguyen et al on 6.949 children in Vietnam in the period from 2000-2008 to identify the effectiveness of vaccination that the prevalence of HBsAg(+) was dramatically higher (5.47%) than whom were born in health facilities (2.25%) (PR: 2.43, CI:1.68–3.51)[72]. Geographical factor appearance was considered as an issue for proportion of HBV infection and Hep BD coverage. In Cambodia, Indonesia, and China, there was a linked between low HepB-BD coverage and home births delivery[88-90]. Following Bunsoth Mao et al's study about the prevalence of chronic hepatitis B virus infection after implementation of a hepatitis B vaccination program among in 1196 children in three provinces in Cambodia, 2011 demonstrated the number of infants who were born in health facilities with SBA, children born at home without a SBA were more likely not to have received a timely BD (aRR=1.94; 95% CI=1.75–2.15). Additionally, the risk of not receiving a timely BD was also greater among children born at home with an SBA when compared with children born in a health facility with an SBA (aRR = 1.54; 95% CI = 1.32–1.80). The reality explanation for this reason because of far distance (remote province) between home and health center, childbearing women may not reach to the health center on time and timely BD for a baby

delivered without an SBA at home requires the mother to visit a health facility within 24 hours of delivery which can be challenging[88]. Sharing the same difficulty, Indonesia experienced HepB-BD challenge in their country, which the majority of delivery was at home, approximately 94% and most of those were attended by TBAs (in Lombok). There was only less than 5% deliveries were attended by a midwife or nurse, who gave the HepB-BD. Even though they had trained injection-givers were attended to the deliveries, who can give a HepB-BD immediately, the results still remained a substantial missed opportunity to provide timely immunization, 39% infants were immunized on the 7th date[89].

It showed a higher prevalence of chronic HBV infection among children delivered at home than those born at large hospitals in China and Vietnam, which emphasized the importance of timely delivery of HepB-BD[72, 91]. Fuqiang Cui and Lili et al made a cohort study aiming to evaluate factors associated with effectiveness of the first dose of hepatitis B vaccine in China from 1992 to 2005 and demonstrated the positive correlation between HBs-Ag positive status and place of birth (at home: OR=2,52; 95% CI=186-3,43 ;p < 0,001 and township: OR=1,54; 95% CI=1,17-2,03; p = 0,002)[91].

In 2015, study of Kenichi Komada et al about chronic hepatitis B through seroprevalence as determined from dried blood spots, among 911 pairs of children and their mothers in central Lao People's Democratic Republic showed the prevalence of hepatitis B vaccine in immunization program was 87%. The number of children whose mother's HBsAg positive was 11 out of 21 children, reached at 52,3%. The maternal HBsAg positivity and being born in a non health facility in children shared the similar positively associated with hepatitis B infection[86].

5.2.2.2. Attendant for delivery

Most of attendant for delivery for both age-groups were health staff such as medical staff (75.2%); traditional birth attendant (17.8%) and family members & relatives (8.4%). However, the prevalence of HBsAg (+) in family members & relatives sector (≥ 18 years old:13; 12.62% and <18 years old: 3; 4.17%) was the highest, then mother herself sector (≥ 18 years old:1; 11.11%); group having traditional birth attendant (≥ 18 years old:

26; 9.25%) and <18 years old 7; 7.87%), medical staff attendant (≥ 18 years old : 52; 9.09%) and <18 years old: 16; 1.62%). We expect that medical workers will have more experience and knowledge to reduce the transmitting of HBV during delivery from mother to their children than family members or relative. Moreover, a study of assess the ability of control HBV infection in Eastern Mediterranean by WHO of Robert D et al indicated 62% of all birth in EMR was born in health institutions with 67% medical staff's support in 2014. However, countries without universal HBV birth dose, only 49% of babies' delivery in health institution with 54% medical staff attendant, compared with 86% and 92% respectively in nations have universal HBV birth dose[92].Plus, the chance of newborn receiving hepatitis B vaccine within 24 hours after delivery was higher if they were delivery in health facilities with medical staff[93].

5.2.2.3. Reason for choosing this delivery place

The convenience (≥ 18 years old: 218; 22.8%) and <18 years old: 185; 16.5%) and mother and child safety (≥ 18 years old: 253; 26.5% and <18 years old: 555; 49.6%) are privilege reason for choosing delivery places. The prevalence of HBsAg (+) was highest in complicated case (in ≥ 18 years old group (4;19.05%) though this figure in < 18 years old group was financial and external condition (4;9.52%). Oppositely, Prahlad Rai Sodani et al. measured 561 patient satisfaction in reasons for choosing health facilities (76-86%, depending on DH, CHC, PHC, etc,….) mostly focus on quality of infrastructure more than skilled medical staff[94].

5.2.3. Hepatitis B infection risks

5.2.3.1. Blood transfusion

Blood transfusion did not exist in many ≥ 18 years old participants (880; 92.5%), though the prevalence of HBsAg (+) in group having blood transfusion was higher 2.26 times comparing to group having no blood transfusion (20%; 8.86% respectively). The study implemented in 904 residents in rural area of Thai Binh province, Vietnam in 2007 by Van

Nguyen et al shares the resemblance trend with our result, indicated the prevalence of HBsAg(+) people having blood transfusion was 88.9%(OR: 3.55, 95% CI: 1.06-11.90)[8].

5.2.3.2. Tattoo

E.R. Miller et al showed the prevalence of HBsAg(+) in participants having tattoo (36.9%) higher than people never had (30.7%)(RR: 1.2, 95%CI : 0.89-1.62) in a network of injecting drug users in Melbourne, Australia[95]. Reversely, our results shared the different trend as ≥ 18 years old participants group having no tattoo with (897; 93.8%) but its prevalence of HBsAg (+) was higher comparing to group having tattoo (9.25%, 6.78% respectively). We basically concluded that the prevalence of HBV infection in Vietnam was high even people do not get any risk from transmitted factors above, the probability of expose to HBV could be possible.

5.2.3.3. Frequency of surgical operation

The proportion of population never have had surgical operation (n=682; 71.6%). The prevalence of HBsAg (+) was higher progressively as the increasing of the number of surgical operation times (never: n= 62; 9.09%; once: n=15; 9.15%; twice or more: n= 9; 10.59%). Similarly, Maria Gancza et al's study about serosurvey on hepatitis B vaccination uptake among adults patients from GP practice in a region of South – West Poland in 2013 showed the higher immunization rate in patients who had surgery before (64,4%) than those not having surgery(35,5%) (OR=2,73; 95% CI= 1,697- 4,433; p< 0,0001). The majority reasons of this figure because of HBV immunization (57,7%) and recommendations by GPs (4,8%)[96].

5.2.3.4. Family member have Hepatitis B

Mostly, people have no family members having Hepatitis B (642/956). The prevalence of HBsAg(+) was the higher in participants group having Hepatitis B (28; 30.43%), as 5.4 times compared with the group have no Hepatitis B (36; 5.61%), However, the positive status of HBV infection in group do not know their family status was significantly (23; 10.36%). Study of Son Huy Do et al conducted in 509 adults participants from 20-81 years old in Binh Thuan province, Vietnam, 2012 indicated the HBs Ag

seropositivity was related to family history of liver disease in both the univariate analysis (OR = 3,1; 95% CI= 1,9–5,3; *P* < 0.0001) and the multivariate analysis (adjusted OR = 3.0; 95% CI, 1.7–5.2; *P* < 0.0001) respectively[84].

5.2.4. Vaccination

5.2.4.1. Vaccination history

There are prominent number of having vaccination in both age-groups (≥ 18 years old (n= 634; 66.33%); <18 years old (n= 1066; 95.21%). The prevalence of HBsAg(+) in group ≥18 years old (n= 82; 8.58%) was higher than group <18 years old(n= 25; 2.19%); and the prevalence of HBsAg(+) in participants have no historical vaccination in group ≥18 years old(n= 32; 15.09%) was higher than group <18 years old(2; 10%); and this prevalence was higher as well above twice comparing to group having historical of vaccination (≥ 18 years old: n=5 0; 7.89%; <18 years old: n= 23; 2.16%).

5.2.4.2. Vaccination site

Health station was the most popular place for vaccination out of options (73.1%), followed by hospital (8.5%) for both age groups. Because, EPI normally conducts in health stations and health centers to create opportunity for every children can reach immunization. Hence, the prevalence of HBsAg (+) in health center was the highest (≥ 18 years old:n= 6; 12%); <18 years old: n= 1; 2.17%); but the second position is in health station (≥ 18 years old: n= 44; 7.97%; <18 years old: n= 21; 2.14%); hospital has the proportion of positive cases (≥ 18 years old: 2; 6.25%; <18 years old: n= 1; 0.69%).

5.2.4.3. Availability of immunization cards

Notably, the absence of their immunization card (86.7%) was high in both age-groups, which the prevalence of HBsAg (+) in this group was (≥ 18 years old: n= 87; 9.15%; 9 times higher compare to group having immunization card; <18 years old: n= 19; 2.28%; quite equal to group having immunization card (n= 6;2.11%)).

In general, Vietnam had been being one of the top countries having high HBV infection prevalence worldwide. Regarding ≥ 18 years old group, the prevalence of HBsAg (+) in group having no historical immunization was as obviously higher two times as having

historical immunization group, while it maintains quite equal prevalence in <18 years old group. Possible hypothesis can explain for figure because this age group was born in the period of beginning the EPI and trial period since 1980, hence the proportion of children have adequate vaccination at that time was lower than this figure in current. Plus, a huge number of absence immunization cards prove for awareness of keep tracking of vaccination doses. According to Yen-Hsuan Ni et al investigated on 1916 persons from 0 to 20 years old before the mass vaccination program in Taipei, Taiwan, 1999 that missing vaccination card was popular in the older age group and vaccination coverage rate was higher in children under 15 years old than who are over 15 years old ($p<0.001$)[97].

5.2.5. Immunization in 12-48 months old in Central region, Vietnam

The number of children not having Hepatitis B birth dose was very high, which indicated the highest prevalence of HBsAg (+) in this group comparing to other groups. Proper time immunization doses tended to increase, especially in Hep 2 (n=132, 50%) and Hep 3 (n=109, 41.28%). However, the number of those having no immunization is still high dramatically, range from 37-57%. The prevalence of HBsAg (+) was increasing gradually in improper time immunization group (0%-3.77%) and remained quite steady in both groups: proper time immunization (0.92%-1.52%) and no immunization (0.98%-1.99%), respectively.

The number of infants having vaccination was low, at n=96, 36.3%. The prevalence of HBsAg(+) of children having birth dose accounted for 1.04%, which was lower than those did not have birth dose, at 1.99%. Among 4 Hepatitis B doses, Hep1 got lowest proportion in 2 sectors: proper time immunization (26.5%); no immunization (37.1%) but highest in improper time immunization sector (36.7%). Hep 2 and Hep 3 shared the resemblance trend of growing proper time immunization doses, though group of having no vaccination group with high proportion. Conversely, Dao et al studied among children in the period from 2000-2011 indicated the children under 5 years old have low timely completion, especially for HBV dose 2 and HBV dose 3, which decreased between

2000 and 2011, though this figure increased in the first dose of HBV at the same period. Particularly, whose mother did not get at least primary school[98].

There had no case positive with HBsAg (+) with proper time immunization and adequate vaccination (3.13%) and 3 cases (1%) had positive with HBsAg (+) with improper time immunization and (or) inadequate vaccination. Possible hypothesis might be explained due to priority of parents mainly worked on agriculture sectors or blue-collar and housework without time arrangement, so they cannot take their children to vaccinate on time. Besides, we can evaluate the role of proper and adequate vaccination (including HBV birth dose and 3 doses polyvalent vaccines in an early stage of life), protecting children against to HBV infection as well as declining the prevalence of HBsAg (+) in community. It primarily can explained that the subjects were too young to have HBsAg(+) and we need to follow up until their adulthood to detect in a longitudinal research.

5.3. ATTITUDE FACTORS AFFECTS TO USING HEALTH CARE SERVICES OF PARTICIPANTS IN CENTRAL REGION, VIETNAM

5.3.1. Intended delivery place for next pregnancy and consultant for health problem

5.3.1.1. Intended delivery place for next pregnancy

Most people chose health facilities for their/ their wife next pregnant, in which the prominent choice go for hospital with 56.33%; health station was the second selection out of places (7.53%) and health center (3.97%). The prevalence of HBsAg (+) in group choosing hospital (51; 9.46%) and house (3; 11.11%). Recently, people aware of the importance of delivery in health facilities to secure their birth labor and reduce the risk of getting infection. Besides, the number of participants still asked for deliver in their house was existing. According to Vanphanom et al invested in rural Laotians for choosing home deliveries over health facilities because of finance burden, distance between health facilities and their house as well as the attitude of health staff and wishing of traditional birth practice[99].

5.3.1.2. Consultant for health problem

Population usually came to medical staff for asking consultant (n=726;75.9%) with lofty HBsAg (+) (n=69; 9.5%), though this figure for partner (n=168; 17.6%; HBsAg (+):n=19; 11.31%) and other family members (n= 227; 23.7%; HBsAg(+): n=22; 9.69%) and friend (n=30; 3.14%; HBsAg(+): n=3; 10%) were also admired. Possible hypothesis for this issue that mostly Vietnamese do not have routine of medical check-up annually. Similarly, to other disease, hepatitis B patients come to see health workers when their symptoms appears, and the prevalence of HBsAg (+) of this sector was quite high. However, family members normally played an important role in giving consultant following our custom.

5.3.2. Reason for refusing health care services and common diseases are refused by financial and qualification condition.

Most of participant had no problem of access health services in light of financial condition (n= 865; 90.48%) and quality condition (n= 921; 96.3%), the number of participants refuse to use health services are quite low in both above groups. The prevalence of HBsAg (+) was highest in group have no health problem (F:10.25%; Q:19%) because they supposed to be healthy until the symptoms appears.

Apart from mentioned diseases, cancer was the most popular disease (0.93%; 0.3%) with the highest HBsAg (+) F:22%; Q: 33% respectively. Other diseases were mostly minor positive HBsAg(+). The quality of cancer treatment in Vietnam does not get the high belief from patient, especially in provincial levels and lower. Besides, cancer costs amount of patient's expenditure, especially for low income people. They usually use traditional remedy instead of medical treatment.

5.3.3. Information acquisition channel about immunization schedule and immunization day for children of participants in Central region, Vietnam

Information acquisition channel about immunization schedule and immunization day for children from medical staff (n=600, 62.8%; n=448, 46.9% respectively), village health volunteer (n=445,46.5%; n=286, 29,9% respectively), immunization card (n=112;

12.65%, n=17; 1.78% respectively). In Vietnam, medical staff will send the invitation letter for parents to take their children for vaccination.

The prevalence of HBsAg (+) was the most prominent in receiving this information from media (radio, internet, TV) (immunization schedule 13.64%) and immunization card (immunization day for children: 17.65%), followed by getting from friends/ family members (immunization schedule 13.3%; immunization day for children: 10.53%).

5.3.4. Person make vaccinated decision

Mothers who take responsibility for making vaccinated decision was 468 out of 924 participants (48.7%). The prevalence of HBsAg (+) in mother sector (n=41, 8.8%); both mother and father (n=29, 10.58%) while grand-parents sector did not have any case. Besides, the others sector (single) was significant attention among sector with the high prevalence of HBsAg (+) (n= 75; 9.41%)

5.4. ASSOCIATION BETWEEN SEVERAL FACTORS AND PREVALENCE OF HBSAG POSITIVE IN CENTRAL REGION, VIETNAM

5.4.1. Age

The proportion of participants in age group under 18 years old having lower chance to get HBsAg (+) 0.228 times, compared to the age group $\geq$ 18 years old. In a national survey about sero-prevalence of hepatitis B infection in 965 participants from 2-90 years old in Nigeria of Adebola T. Olayinka et al, the percentage of people who were at risk of HBV infection declined momentously with the increasing age ($\chi 2$ for linear trend = 29,2 ; $P < 0.0001$)[100]. However, Tatiana Balaeva et al conducted study on seroprevalence of markers of HBV infection, a population- based in 1243 young adults in Arkhangelsk, Northwest Russia, which had two times higher of the prevalence of serological of HBV among participants aged 30–39 years compared to those aged 18–29 years[85]. It also showed the same tendency for anti-HBc for those age-groups, at 22,8 and 10,6 respectively in 6,217 volunteers in Moscow region who were observed after 10 year conducting mass infant vaccination against HBV[101]. Melo. L et al implemented epidemiological study of

hepatitis B and C in a municipality with rural characteristics: Cássia dos Coqueiros, State of São Paulo, Brazil in 2015, which divided 1001 participants into six age-groups from 18 to over 64 years old. It depicted a progressive increase in positivity with HBV by age (p = 0,009) which the most prominent age-group was 55-64 years old (8,4%)[102]. Study of Son Huy Do et al conducted in 509 adults participants from 20-81 years old in Binh Thuan province, Vietnam, 2012 presented the HBsAg positive prevalence was lower following the decrease with age, which was related to age of 50 years or over (OR = 0.3; 95% CI, 0.1–0.6; $P < 0.001$), while HBV exposure was associated with age of 40–49 years (OR, 1.8; 95% CI = 1.0–3.0; $P < 0.05$) and age of 50 years or over (OR= 1.8; 95% CI = 1.1–3.1; $P < 0.05$) in univariate analysis. Multivariate analysis identified that HBsAg seropositivity was related to age of 50 years or over (adjusted OR = 0.3; 95% CI= 0.1– 0.6, $P < 0.001$), whereas HBV exposure was still associated with age of 40–49 years (adjusted OR = 1.8; 95% CI, 1.0–3.1; $P < 0.05$) and age of 50 years or over (adjusted OR = 1.8; 95% CI, 1.1–3.1; $P < 0.05$)[84]. Our study partly presented the efficiency of vaccination, when most of participants over 18 years old did not have chance to immunization adequately in their childhood, resulted in the prevalence of HBsAg (+) higher in this groups, comparing to the group under 18 years old.

5.4.2. Attendance for delivery

There was an association between the prevalence of getting HBsAg (+) to participants whose delivery had attend of medical staff (OR:0.489, 95% CI: 0.330-0.725, p<0.001); traditional birth attendant (OR:2.015, 95% CI: 1.321-3.076, p=0.001); family member & relatives (OR:1.891, 95% CI:1.087-3.289, p<0.05) comparing to those who did not have these attendants. In our study, we found the important role of medical staff who has experiences and skills in support delivery, lead to the prevalence of HBsAg (+) in this group was lower. However, the birth delivery having attend of traditional birth attendant and family member and relatives, which enhanced the prevalence of HBsAg (+) in community. Possible hypotheses explain that those people do not have enough skills as well as other method of preventing infection, including HBV. According to Robert D.

Allison et al in his study about “Hepatitis B vaccine birth dose coverage correlates worldwide with rates of institutional deliveries and skilled attendance at birth”, collected individual country data on the latest IDR and SBA rates reported by each country in 2017, it indicated significant positive correlations between HepB-BD coverage and IDR (rho = 0.42, $p < 0.001$), SBA rate (rho = 0.44, $p < 0.001$), the density of hospital (rho = 0.33, $p = 0.02$) and total health expenditure per capita (rho = 0.24, $p = 0.03$) in worldwide. Additionally, IDR also has a high correlation with SBA (rho = 0.94, $p < 0.001$) and adults literacy rates (rho = 0.52, $p < 0.001$) respectively[103]. Hang Pham et al implemented a study to evaluate knowledge, attitude and practice of hepatitis B prevention and immunization in 380 pregnant women in the range of 17 to 45 years old who lived in two northern provinces Vietnam. Regarding to place taking delivery, giving birth at province level hospital was independently associated with maternal antenatal HBV screening uptake (OR= 6,61; 95% CI = 2.04–21.45) and the proportion of HB immunization in infant (OR= 4.39; 95% CI= 1.48–13.02)[104].

5.4.3. Reason to choose delivery place

Participants tended to choose health facilities due to their delivery risks, such as heart disease, infectious factors, and concerned about the successful of birth delivery. The proportion of participant having their own individual selection getting HBsAg (+) was higher than complicated case sector, at 2.264 times. Possible hypothesis can explain within the complicated cases, participants chose health facilities for reducing the risk of their delivery and also decline the possibility of HBV transmit. Then with group of individual selection, it might had more risk of increase the high contagious factors if their choose delivery place like home, or others place different from health facilities.

5.4.4. Family member status of Hepatitis B

The proportion of participants did not have and did not know their family member status of Hepatitis B having chance to get HBsAg (+) was higher 3.861 times and lower 0.518 times respectively, compared to the group of participants known their family member status respectively. Peng Huang et all studied on seroepidemiology of HBV infection and

impact of vaccination collected randomly and investigated 148.931 individuals by multistage random sampling in Eastern China. There was a relation between the higher proportion of HBsAg positivity and the lower of participants whose without familial history of HBV ($p<0.005$). Furthermore, 12.016 out of 148.931 participants had familial history related to HBV infection (8.28%, 95%CI: 8.14%-8.43%), which analyzed separately into different classes showed a statistically significant increase for mothers, fathers, spouses, offspring and siblings to HBV infection risks[83]. Ala U Tokan's study also presented the relevant between HBsAg(+) and the number of HBV carrier in family that among single HBV carrier got 57 percent while this figure among families having three or more HBsAg(+) members was 98%, irrespective of family size ($p < 0.05$). It also indicated a trend toward a greater HBV proportion in children whose mothers had HBsAg-positive than those had HBsAg-negative[105].

5.4.5. Vaccination history

Our study showed the proportion of participants did not know their vaccination history getting HBsAg (+) was higher than those who have vaccinated before, at 4.739 times. Hsien-ChengChang indicated in her study about seroprevalence of Hepatitis B viral markers among 7592 freshmen from one university in Northern Taiwan participated in entry health exam in September 2003 and September 2004 to evaluate 20 years after mass Hepatitis B Vaccination Program in Taiwan. The seronegative rate was 21.5% in subjects with self-reported hepatitis B vaccination history, and 38.9% in those without self-reported hepatitis B vaccination history. In addition, the seronegative rate of subjects born before July 1984 and after July 1984 was 19.2% and 21.8% in subjects with self-reported hepatitis B vaccination history, and 33.5% and 41.5% in those without self-reported hepatitis B vaccination history, respectively ($p < 0.001$) [106].

5.4.6. Availability of immunization cards

The proportion of participants having no immunization card getting HBsAg (+) was higher than those who had immunization card, at 2.988 times. With available of

immunization card, participants can keep track of the vaccination schedule and vaccinate adequately, hence it helps to reduce the prevalence of getting HBV infection. In study of Dambadarjaa Davaalkham about Serology results was conducted in 1,145 children (592 boys and 553 girls) aged 7-12 years (survey response rate: 93%) that the proportion of subjects having HB vaccine among those having immunization cards accounted for 60.1%, and approximately of 65% children had received the birth doses on time whereas the remaining subjects received the birth dose late (31.9%) or birth doses of HB were not administered (3.4%)[107].

5.5. LIMITATION

Our study was just included the specific Central Region, which may not represent the whole country. Since children from 12-24 months old provided low immunization card availability, it is difficult to draw any conclusion about the severity of HBsAg (+) among children in the community. Further studies involving which some essential issues (income, tattoo), lead to participants denied answering.

5.6. FURTHER RESEARCH

Regarding the overall prevalence estimates of particular participants in Central Region of Vietnam, the problem of sampling bias should not be underrated. The prevalence of HBsAg(+) in adult was considerable high; however, with the development and stable of EPI which help to reduce the proportion in children in the future. Continued surveillance is needed to monitor changing in Hepatitis B epidemiology before and after vaccine introduction. In addition to monitoring infection, changing the attitude and behavior of population plays important roles to assess whether vaccines are affecting the HBV infection in Vietnam and other high epidemic area.

CONCLUSIONS

Our study suggested that Hepatitis B infection was still a significant cause of among children younger and adult from 1-39 years old in Vietnam.

In the context of low vaccine proportion or uncertain their historical vaccination, and the HBsAg (+) prevalence is mostly in the adults; getting a full schedule of Hepatitis B vaccine and checking the status are very important, in particular, population who have not had chance to approach vaccination due to their external condition during their childhood and their behavior comparing to children.

We also observed with the univariable regression logistic model and Chi-square, there are relevant factors with the prevalence of HBV infection in the population, including:

- Age group: <18 years old (OR: 0.228, 95% CI: 0.145-0.359, p<0.001)
- Attendant for delivery: Medical staff (OR: 0.489, 95% CI: 0.330-0.725, p<0.001); Traditional Birth Attendant (OR: 2.015, 95% CI: 1.321-3.076, p=0.001); Family member & Relatives (OR: 1.891, 95% CI: 1.087-3.289, p<0.05)
- Reason to choose delivery place : Individual selection (OR: 2.264, 95% CI: 1.045-4.904, p<0.05)
- Family member have Hepatitis B: No (OR: 3.861, 95%CI: 2.079- 7.171, p<0.001;); Unknown(OR: 0.518, 95% CI: 0.30- 0.895, p<0.05)
- Vaccination history: Unknown (OR: 4.739, 95% CI: 1.808-12.422, p<0.05)
- Availability of immunization cards: No (OR: 2.988, 95%CI: 1.300-6.867, p<0.05;);

There is a need to consider the community communication to vaccinate frequently in the Expanded Program on Immunization within this dramatic situation.

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